APPENDICES

A CONTINUATION OF

FEASIBILITY STUDY FOR THE MANUFACTURE OF ZERO GRAVITY PHARMACEUTICALS, IMMUNOLOGICAL, AND VIRAL AGENTS

(NASA-CR-120425) FEASIBILITY STUDY FOR THE MANUFACTURE OF ZERO GRAVITY PHARMACEUTICALS, IMMUNOLOGICAL, AND VIRAL AGENTS, APPENDICES (Little (Arthur D.), Inc.) 238 p HC $15.00 CSCL 13H G3/15

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APPENDIX 1

USES OF ELECTROPHORESIS IN BIOLOGY AND MEDICINE (UP TO 1970)

The first recorded use of electrophoresis in protein chemistry was the determination by Michaelis in 1909 of isoelectric points of enzymes. In 1937, Tiselius extended Michaelis' work and refined the moving boundary method of electrophoresis to separate proteins according to their electrophoretic mobility. In this method, also known as "free" electrophoresis, the motion of a boundary between a colloidal solution and the solvent is observed, usually by measuring the refractive index of the solvent along the electric field gradient. Although the technique provides an accurate measurement of electrophoretic mobility, it is difficult to use for separation for clinical or fractionation purposes. Since "free" electrophoresis operates without any supporting media, it is difficult to keep the overlapping boundaries separate; gravitational instability and convection causes mixing of the components, and instability of the moving layers results.

These problems of destabilization of separation zones has been overcome by the use of stabilizing anticonvective media. The preferred approach to stabilization is the use of solid media such as paper, powders, or especially, gels such as starch, agar, silica gel, or polyacrylamide gel. The latter gel is the most widely used medium for protein separation.

With the advent of the stabilizing gel media, the uses of electrophoresis in protein chemistry, and particularly in protein analytical chemistry, have multiplied enormously, until it has become one of the most widely used analytical tools in biochemistry.

Several excellent review articles over the past few years have illustrated the particularly wide diversity of applications to which electrophoresis has been applied, ranging from routine clinical diagnostic applications and basic research into the structure of proteins to the use of electrophoresis in the monitoring of adulteration of food products and to forensic science detection work. The review article of R. D. Strickland (Analytical Chemistry, Vol. 42, No. 5) is particularly comprehensive. In the following sub-sections we briefly survey some of the common uses of electrophoresis in biology and medicine.

A. Clinical and Diagnostic Chemistry

Electrophoretic analysis of body fluids provides a rapid and sensitive method of detecting a number of disorders.

Urinary protein patterns are useful in the diagnosis of a wide range of biochemical disorders and diseases. In cancer patients, a slow-moving

glycoprotein is characteristically present in the urine which is not found in the urine of normal patients.[75] Heavy-chain immunoglobulin fragments may also accompany Bence-Jones proteins in myeloma.[114] Electrophoretic detection has also been used to screen for amino acidurias and for abnormal excretion of amino acids and sugars in urine.[46, 113, 147] Similarly radioiodine coupled with electrophoretic separation has been used to detect and measure picogram amounts of protein in the urine.[70] Urine gamma globulin in elevated amounts is found by electrophoresis in the patients suffering from lupus-erythematosis.[32]

Electrophoresis of cerebrospinal fluid has been used for the detection of multiple sclerosis;[14a] in the active phase of the disease, cells from the cerebrospinal fluid have been shown to produce a unique immunoglobulin which is not found in normal subjects, nor is it found in multiple sclerosis patients during periods of remission of the disease. These findings have provided evidence that the disease is caused by autoimmunity. Other changes in electrophoretic patterns of cerebrospinal fluid proteins have also been found in glycoproteins, and the diagnostic significance of these are currently under study.

Electrophoretic separation and analysis of gastric juice proteins have shown that the albumin level of gastric juice is elevated in anemia, gastric cancer and gastritis. The distribution of proteins and microproteins in duodenal fluid have been shown to be markedly changed in patients suffering from cystic fibrosis.

Electrophoretic patterns of human serum have been used for a number of diagnostic applications. The first sign of liver cirrhosis, for example, is a rise in β_{2A}-globulin, and a new zone in the γ-globulin region of cirrhotic serum has also been shown under special applications.[33, 57] In other types of liver disease, special types of hyper-gamma globulinemia have been shown to occur, and the significance of these is currently under study.[16]

Electrophoretic patterns of maternal serum has been shown to differ in pre-toxemia, and periodic electrophoresis of toxemia-prone pregnant women has been used as a screening test to detect the onset of toxemia as early as possible.[22] Electrophoresis has also been used to detect extremely dilute antibodies in serum, as well as dilute antigens such as gonadotropins.[124] Immunoelectrophoresis has also shown abnormalities in the α, γ, and β globulins in the serum of children with systemic lupus erythematosus.[132]

A great number of other diseases have been shown to give slightly or greatly abnormal electrophoretic patterns in serum. For example, Banti's disease (congestive splenomegaly) has been shown to display lowered albumin content, while globulins are elevated.[126] Niemann-Pick's disease, a hereditary disease characterized by a set of syndromes involving the liver, spleen, lungs, nervous system, etc., results in greatly diminished levels of lipoproteins in serum. Acute tetanus

causes a great increase in α, β, and γ globulins.[149] A number of other electrophoretic tests have been found especially useful in the diagnosis of a range of cancers. Diagnosis of myeloma[115] and differentiation between myeloma and Waldenstrom's macroglobulinemia[38, 122] have relied heavily on electrophoresis. Leukemia leukocytes have been shown to have a unique antigen present,[64] while reversal in the ratio of α_1 to β globulin vitamin B_{12} binding can be detected by electrophoresis, and is used to diagnose chronic myelogenous leukemia.[100]

Generally in many cases of cancer, significantly elevated levels of glycoprotein have been shown in the serum.[8]

Other diseases in which abnormal patterns in serum occur include:

> leishmaniasis (infantile splenomegaly caused by a mediterranean parasite) in which the electrophoretic pattern shows greatly elevated IgG and slightly elevated IgA and IgM[90];
>
> typhoid, in which carriers have been shown to be notably low in IgM and high in IgG[121];
>
> ulcerative colitis, in which α_1 and α_2 proteins have been shown to be elevated, and cryoproteins containing IgG and IgM have been shown to be present[108, 116]

and a variety of other common and obscure diseases.

Electrophoresis has been extensively used for the detection of genetic and disease-induced protein abnormalities in blood, particularly hemoglobin. These include sickle-cell anemia,[80] hemoglobins with diminished[14, 111] and enhanced[60] oxygen affinities, and a variety of other hemoglobin variants[63, 118, 127, 148, 139, 94] which may, or may not be associated with a diseased state.

Immunoelectrophoresis of other body fluids used for diagnostic purposes includes:

> synovial fluid, in which haptoglobin increases have been shown to be associated with arthritis[79], as are abnormal distribution of the lactic dehydrogenases. Measurement of the degree of polymerization of hyaluronic acid in synovial fluid is useful for assessing the effects of anti-inflammatory drugs[62]
>
> amniotic fluid, in which abnormal protein distributions have been used for the detection of toxemia, some congenital fetal malformations and diabetes mellitus[27]

B. Protein Research

Electrophoresis is extensively used in the investigation of the properties of proteins, including a characterization of their electrical charge, their size, and their degree of homogeneity. Serum albumin, for example, has been shown to separate into two distinct components, and several poorly resolved ones [120], and considerable research has gone into the investigation of whether these components represent polymerization or depolymerization, and the factors affecting aggregation.

Vitamin binding studies, particularly in vitamin B_{12}, have actively employed electrophoresis. [49, 56] Most vitamins are bound by the α and β proteins, but albumin has been shown to transport most of the biotin, pantothenate and β-carotene. [11]

Other proteins which have been studied include clotting factors, serum globulins [37, 136, 137] enzymes including deoxyribonucleases [142] glycosidases[87] proteases,[101, 119] cellulases,[2] lactases,[66] carbonie anhydrase[65] etc.

Milk proteins have been extensively studied, using electrophoresis as one of the major separating and analysis tools. [52, 97] Studies have shown that protein content in bovine milk varies from breed to breed [41, 76, 77, 81, 106] and that some protein fractions may be totally lacking in some breeds of cattle[99]. The genetics controlling the variations in milk proteins have been studied in cows [5, 43, 54, 58, 98, 125] and in other species including buffalos[51, 93] sheep [12, 31, 75] and zebus [6]. Human milk has been sown to lack casein present in other mammal milk, while most of the other proteins found in human milk, such as albumin, lipoprotein, glycoprotein, ceruloplasmin, haptoglobin, transferrin, IgA, IgG and IgM [26, 28, 83, 110] have been shown in cows [91, 109], sows [86] and rats.[102] IgA protein has been shown to be present in particularly concentrated amounts.

Electrophoresis has been used to analyze saliva proteins (parotid saliva, for example, has been shown to contain thirty different proteins [133] sweat (where sixteen different plasma proteins have been shown to be present [138] and tears (human tears have been shown to contain a specific prealbumin[15, 67] and an IgA that differs from that of serum.

The interactions of proteins, and complex formation has been actively studied with the aid of electrophoresis. Heparin has been shown to form complexes with gamma-globulin and thrombin, but not with albumin and fibrinogen.[117] This has lent considerable insight into the understanding of the mechanism of this anti-coagulant in preventing clot formation. Hyaluronic acid has been shown to form a complex with serum albumin that is sufficiently stable to appear as a new electrophoretic peak.[105] The interactions of proteins with ions has been extensively studied. For example, the competitive binding of iron with plasma proteins and chelating agents such as ehtylenediaminetetraacetic acid has been studied. The iron has been shown to be removed from

the plasma protein and irreversibly bound to the EDTA.[4] The EDTA chelating agent has been shown to bind to albumin. Fluoride in serum has been shown to be preferentially and irreversibly bound to albumin[134], while calcium binding to serum proteins has been shown to be an equilibrium reaction; the extent of binding depends upon both the calcium and the protein concentrations.[68]

The field of enzymology has made particularly widespread use of electrophoresis in the isolation, purification and identification of enzymes, and a number of general reviews have been written on the subject[85, 89, 146].

In hormone identification and analysis, a technique has been developed for the separation of free and anti-body bound hormones[123]. Electrophoresis has been used to analyze the purity of hormones. Commercial preparations of insulin, for example, have been shown to have several slowly-migrating fractions.[9] Insulin has been shown to circulate in the blood stream bound mostly to α_2- globulin.

C. Detection and Analysis

(1) Food Applications

Electrophoresis has been used in the analysis of a number of commercial food applications to assess purity and protein content. The egg content of noodles can be determined electrophoretically,[129] and the presence of egg white in commercial preparations of egg yolk can be detected.[104a] Electrophoresis is particularly useful--and has been widely used--to distinguish between species of fish in commercial products[30, 36, 84, 88, 135]

Because the types of protein in mammalian milk has been so extensively evaluated (see above), adulteration of one milk with that from another species can be detected. Adulteration of cow milk with goat milk for example [50, 21] or buffalo milk with cow milk [3, 42] has been reported. Similarly, adulteration of cheeses can be detected. Classic Roguefort cheese, for example, is from sheep, while Blue cheese is from cow milk .[7] Adulteration of Roguefort with Blue has been documented. It has been reported that Swiss cheese aging can be followed by observing the variations of its proteins.[40]

Electrophoresis can also be used for the detection of milk protein adulteration of meat products. This is particularly common in meat by-product products such as sausage and meat patties.[130]

Electrophoresis is useful in the analysis of cereal grain products. It has been proposed to replace the inexact "dropping number" method of evaluating bread grains,[112] and has been used to detect the changes in barley proteins in beer fermentation.[55]

In the wine and cider industry, electrophoresis has been used to distinguish between sparkling and carbonated wines by measurement of aspartic and glutamic acid contents[35] and to detect apple cider adulteration of wine.[25]

(2) Forensic Science

Electrophoresis has been particularly useful in the detection of toxins after autopsy.[17] These include digitoxin, barbiturates, and other drugs. A rapid method for identifying bloodstains by immunoelectrophoresis has been developed.[39] Sperm can be identified electrophoretically by its characteristic pattern,[140] by confirmation of the presence of spermine,[24] or by demonstrating the presence of lactic dehydrogenase X.[47]

Toxins such as insecticides have been detected for as long as twelve days after death.[23].

(3) Pharmacology

Electrophoresis has been used in a number of pharmacological applications to measure purity of drugs, and to separate components. It is routinely used to measure purity of plasma protein fractions such as human albumin,[103] gamma globulin preparations, etc.

Anti-biotics such as streptomycin and its derivatives and the erythromycin derivates have been separated by electrophoresis.[73, 72, 82]

In the analysis of compound medicinals, electrophoresis has proved useful for separating the salicylates, barbiturates and alkaloids.[10]

D. Botany

Electrophoresis has been extensively used in the study of the genetics of cereal grains. Both the albumins and globulins of wheat, for example, are extremely heterogeneous [44, 48, 59, 128]; the protein patterns are related to wheat varieties, and can be used to trace the genetics of the wheat strains. Similarly, barley contains proteins which are very heterogeneous[95] as do soybeans and other beans and peas.

Electrophoresis has also been applied to non-protein plant substances including the separation of metal-organic complexes,[61] phosphase esters,[19] amino acids and organic acids.[34] It has also been used for the measurement of bound carbohydrates and other neutral fractions.[85a 34]

Electrophoresis has been applied to soil measurements to study such components as humic acids, [18, 69] iron complexes,[78] and other metal complexes.[1]

E. Microbiology

In microbiology, electrophoresis has been particularly useful in the measurement of different forms of DNA (deoxyribonucleic acid) and RNA (ribonucleic acid.) Virus-specific RNA has been identified in cells infected with polio virus.[107] Infection RNA has been isolated from foot-and-mouth disease virus[92] and the virulent form of bacteriophage λ has been shown to contain less DNA that the non-virulent form.[141]

Protein synthesis has been studied in cell cultures infected with herpes simplex, and it has been shown that the virus causes at least 25 different proteins to by synthesized.[131]

Electrophoresis has been found to be useful in the classification of a variety of microorganisms including Penicillium,[13] Mycoplasma,[145] Phytophthora,[53] etc. Enteric bacteria[20] mycobacteria[104] and a variety of other fungi, plants and other microorganisms have been classified with the aid of electrophoresis.

The proteins of a number of different viruses have been fractionated. These include Newcastle virus,[45] herpes virus,[144] vesicular stomatitus virus 71, [143] tobacco mosaic virus[96] and a wide variety of other viruses responsible for disease in plants, animals and man.

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APPENDIX 2

INDUSTRIAL RESPONSES

TO

ARTHUR D. LITTLE, INC. INQUIRY

ABBOTT

Scientific Division

Abbott Laboratories
North Chicago, Ill. 60064

November 1, 1973

Dr. P.A. Gempel
Arthur D. Little Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Dr. Gempel:

Your letter to Dr. Singiser concerning electrophoresis in space has been transmitted to me for reply.

We are already very much involved in designing experiments of the type you mentioned and I am working with Marshall Space Flight Center now on a possible experiment for the Soyez-Apollo Flight in 1975.

I'm not sure what this would mean in regards to your program, but if you would like to discuss it some time please let me know.

Sincerely yours,

Grant H. Barlow

Grant H. Barlow
Molecular Biology Research

GHB/cm

MERCK SHARP & DOHME / RESEARCH LABORATORIES

DIVISION OF MERCK & CO., INC. RAHWAY, NEW JERSEY 07065 · TELEPHONE (201) 381-5000

RONALD A. ROSENBERGER
ASSISTANT TO THE PRESIDENT

October 22, 1973

Mr. P. A. Gempel
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Mr. Gempel:

Thank you for your recent letter to Dr. Sarett regarding the NASA project you have been contracted to undertake. Dr. Sarett asked that I inform you that we will consider the information you supplied and the questions you raised at the next monthly meeting of our Research and Development Council. Since the Committee will be meeting later this month, we should be in a position to reply sometime in November.

Thank you for your interest in the Merck Sharp & Dohme Research Laboratories.

Sincerely,

Ronald A. Rosenberger

MERCK SHARP & DOHME / RESEARCH LABORATORIES

DIVISION OF MERCK & CO., INC. RAHWAY, NEW JERSEY 07065 · TELEPHONE (201) 381-5000

RONALD A. ROSENBERGER
ASSISTANT TO THE PRESIDENT

November 20, 1973

Mr. P. A. Gempel
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Mr. Gempel:

Our Research and Development Council has considered the information you supplied regarding potential space projects. In order to explore several ideas in more depth, it was referred to our Basic Research area here in the Merck Sharp & Dohme Research Laboratories. Since I indicated we expected to reply sometime in November, I am writing to let you know that it will probably be several more weeks before we will be in a position to provide a definitive reply and that Dr. David P. Jacobus, our Vice President for Basic Research or one of his colleagues will be writing you directly.

Sincerely,

Ronald A. Rosenberger

Ronald A. Rosenberger

MERCK SHARP & DOHME / RESEARCH LABORATORIES

DIVISION OF MERCK & CO., INC. RAHWAY, NEW JERSEY 07065 · TELEPHONE (201) 381-5000

DAVID P. JACOBUS, M. D.
VICE PRESIDENT FOR BASIC RESEARCH

15 January 1974

Mr. P. A. Gempel
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Mr. Gempel:

This letter is to follow up your letter of 17 October 1973 to Dr. L. H. Sarett and Mr. R. A. Rosenberger's acknowledgement dated 22 October 1973.

You have asked us to identify a substance of potential importance which would be best isolated using electrophoresis under zero-gravity conditions. At present, we are not able to suggest a substance that has not yielded to examination using terrestrial techniques. The problem is made more difficult for us because we believe that a system equivalent to zero gravity can be achieved in an ultracentrifuge using diffusion across an equilibrium boundary. Such a system could then be subjected (we have not) to electrophoresis.

There are two other areas which might be of potential interest for an experiment in space if they have not already been adequately explored.

The rapid and profound demineralization is apparently comparable to the demineralization seen in fracture immobilization and in prolonged bed rest. On earth these changes take place so slowly that the factors affecting the demineralization have never been properly identified. The non-exercise situation in space might provide a sufficient change in the levels of the factors involved (calcitonin, somatomedin, growth hormone, vitamin D, etc.) so that the non-exercise situation could be unravelled.

The second area in which I suspect the Space Agency has done work deals with the examination of the circadian rhythm since the astronauts are undoubtedly on a special space schedule. Following the pattern of their biological clock by different metabolites in the urine might provide an insight into normal circadian rhythms as well as perhaps assist in developing appropriate schedules for future flights.

Please let us know if we can be of further assistance.

Sincerely yours,

David P. Jacobus

DPJ:ht

LEDERLE LABORATORIES

A Division of AMERICAN CYANAMID COMPANY
PEARL RIVER, NEW YORK 10965
AREA CODE 914 735-5000

November 30, 1973

Dr. P. A. Gempel
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Dr. Gempel:

Thank you for your letter of October 17, regarding the interest of NASA to study the potential benefits to mankind of isolating or purifying biochemical, immunological or viral agents in space. Your correspondence has been circulated to members of our research staff, but I regret that we are unable to suggest any appropriate experimentation.

Sincerely yours,

Ira Ringler
Director of Research

IR:cam

Ayerst

AYERST LABORATORIES
DIVISION OF AMERICAN HOME PRODUCTS CORPORATION

685 Third Avenue / New York, N. Y. 10017 / Tel: (212) 986-1000 / Cable: ALPHAMIN, New York

C. J. CAVALLITO, Ph. D.
EXECUTIVE VICE PRESIDENT

October 19, 1973

Mr. P. A. Gempel
Arthur D. Little, Inc.
Acorn Park
Cambridge, Mass. 02140

Dear Mr. Gempel:

Thank you for your letter of October 17th in which you describe the substance of your contract with the National Aeronautics and Space Administration to study certain operations in space.

I have forwarded copies of your letter to our Research and Development administrators who will discuss your interests with others of their staffs to see whether there are some projects or experiments that could be suggested to you.

Thank you for your interest.

Sincerely,

C. J. Cavallito

CJC:chh

cc: R. Deghenghi
S. M. Olin

THE DOW CHEMICAL COMPANY

POST OFFICE BOX 68511
INDIANAPOLIS, INDIANA 46268

317 638-2521
CABLE: DOWPHARM — INDIANAPOLIS

November 27, 1973

Mr. P. A. Gempel
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Mr. Gempel:

Thank you for your letter of October 17, 1973 in reference to your program to study the potential benefits to mankind for isolating or purifying biochemical, immunological, or viral agents in space. We appreciate your extending to Dow the opportunity to participate in this program, but after examination of all our projects, we do not have one which we feel would qualify at this time for this program. If, in the future, we do have something suitable, we will contact you.

Thank you again for your consideration.

Sincerely,

Anton J. Schwarz, M.D.
Director of Biological
Research and Development

AJS/jw

ORTHO RESEARCH FOUNDATION
RARITAN, NEW JERSEY 08869

October 25, 1973

Mr. P. A. Gempel
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Mr. Gempel:

Your letter dated October 17, 1973 to Dr. Cronk was referred to me for reply. I took the liberty of discussing the programs which you have under contract with the National Aeronautics and Space Administration with a few of my Division Directors and, although they were intrigued with the scope of the work, they failed to see how we could contribute to the project. I must, therefore, respectfully decline your offer to work with us.

We do thank you, however, for thinking of Ortho.

Sincerely,

John P. DaVanzo

John P. DaVanzo, Ph.D.
Executive Director of Research
Basic Sciences

JPD:v

NARREN-TEED PHARMACEUTICALS INCORPORATED

82 WEST GOODALE STREET, COLUMBUS, OHIO 43215
(614) 221-5574

AMUEL GUSMAN
RESIDENT

November 7, 1973

Mr. P. A. Gempel
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Mr. Gempel:

Thank you for your October 17 letter regarding electrophoretic studies under conditions of "zero g". There are no such studies which I have in mind at the present point; hence, I have no suggestions.

However, it has occurred to me that perhaps some of my associates at the Rohm and Haas Company may have some experiments in mind, and I am taking the liberty of forwarding a copy of your letter to them. Should there be any interest on their part, they will take the initiative in contacting you separately.

I found the proposal in your letter quite interesting and very much appreciated hearing from you.

Sincerely yours,

Sam Gusman, Ph.D.

gm

THE UPJOHN COMPANY

KALAMAZOO, MICHIGAN 49001
TELEPHONE (616) 382-4000

November 19, 1973

Ms. Pat A. Gempel
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Ms. Gempel:

I have consulted with the Manager of my unit, Dr. E. S. Gerard, and have been advised that company policy has been developed to deal with contract research. Higher management decides which concepts could be developed within the framework of the Corporation and which concepts would be best developed outside of our immediate resources.

A great number of applications of electrophoretic techniques can be cited as beneficial to mankind. My contribution to such a program would first need to be funneled through the channels; however at this point I would like to receive more information about specifics of contract relationships, and the type of consultation and guidance that you would be seeking outside of a contract relationship. A great number of clouding issues are raised by such an involvement. Clearly most efforts to solve a biological problem require the coordinated efforts of many portions of society, industry, non-profit public and private research foundations, universities and the government. I would be interested in participating in such a coordinated effort and would serve as an advocate within the company structure to try to balance profit motivation; exclusivity, legal responsibility with a cooperative venture with individual contributions and responsibilities defined. I believe that some of the fears that exist would be decreased if there was a clear understanding of the individual roles in such a venture, along with some prior legal understanding of the degree of sharing to take place in the return in investment that occurs.

I will be happy to discuss further scientific concepts upon receipt of additional information and company approval.

Sincerely,

Clifford L. Kragt, Ph.D.
Fertility Research

CLK:mem

MARION LABORATORIES, INC.
10236 BUNKER RIDGE ROAD • KANSAS CITY, MISSOURI 64137

October 24, 1973

Mr. P. A. Gempel
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Mr. Gempel:

I am in receipt of your letter dated October 17, 1973, to Dr. Zuber of this organization.

The potential benefit that could result from a project such as you describe is certainly tremendous and I am sure that many new avenues of research could open up even in the initial stages of the project. However, this is an area in which Marion Laboratories is not involved and most likely will not be involved with in the immediate future.

We appreciate your consideration and hope the results of your work prove to be most beneficial.

Sincerely,

MARION LABORATORIES, INC.

Lowell D. Miller, Ph.D.
Scientific Director

LDM:pd

APPENDIX 3

MEDLAR LITERATURE SEARCH REFERENCES

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APPENDIX 4

STUDIED DURING PERFORMANCE OF THIS EVALUATION

(Reference numbers refer to Medlar Search)

Substance Analyzed	Reference Number
A-Component from Bovine Insulin	872
ABO Antigens on Human Lymphocytes	615
Abnormal Lipoprotein (LP-X)	395
Abnormal Fibrinogens	580
Acid Alpha L-Glycoprotein	121
Abnormal Factor X	1074
Acid Phosphatases	1093
Acidic Glycines	791
Aconitase	653
Acute Infectious Hepatitis	327
Acyl Phosphatase	389
Adenosine Deaminase Gene	514
Adenovirus Penton Base Antigen	503
Adenovirus-Specified Thymidine Kinase	113
Albumin	339
African Swine Fever-Antibody	550
Alcohol Dehydrogenase Isozymes	608
Aldehyde Dehydrogenase	690
Alkaline Phosphatase Enzymes	487
Alkaline Phosphatase Isoenzymes	937 1112 696
Alkaline Proteases	1104
Alkaloid Mixtures	378
Allergen Extracts	1014
Allergens	441 704
Alpha-Feto-Protein	138 456
Alpha-Lipoproteins	244
Alpha-Mannosidase	577
Alpha 1	1058

Substance Analyzed	Reference Number
Alpha 2-M-Feature	922
ALS and Prednisolone	16
Amebiasis	894 961
Amino Acid	18 23 84 160 740 930 452 713
Amino Acid Patterns in Blood Serum	84
Aminoacyl Transferase	205
Amino Groups in Chymotrypsinogen A	313
Aminopeptidases of Basidomycetes	1069
Amphetamine Isomers	556
Ampholines	418 845
Ampholytes	197
Amylase-Starch	196
Angiotensin I Converting Enzyme	594
Antibody	738 1055
Antibody-Sensitized Red Cells	741
Anti-D Immunoglobulin	211 969
Anti-Estradiol Antibodies	225
Anti-Gamma G-Globulin Blood Stains	464
Antigenic Extracts of Aspergillus Flavus	802
Antigens	1055
Antigens of Trichinella Spiralis Larvae	27
Antihapten Antibodies	1057

Substance Analyzed	Reference Number
Anti-Lymphocyte Serum	48
Apoproteins	854
Arginase Isoenzymes	209
Arginine Esterase	596
Arginine-Rich Histones	981
Aromatic Amines	370
Arteriosclerosis	707
Aspartate Aminotransferase Isoenzymes	1002
Aspartate and Alanine Aminotransferase	698
Aspergillosis	927
Aspergillus Niger Beta-D-Xylosidase	242
Aspergillus Precipitins	946
Atopic Allergen in Hen's Egg	353
Atopic Individuals	298
Aujeszky Virus	744
Australia Antigen	193 289 308 263 358
Autoantibodies	904
Autoradioimmunoelectrophoresis	460
Avian Ribonucleic Acid Tumor Virus Group-Specific Antigens	762
Bacteriophage DNA	637
Bacterial L-Forms and Mycoplasma	398
Bacteriophage Q Intact Virions and Viral Proteins	467
Beagle Serum Proteins	257
Beta-Glucoronidase in Human Sera	31
Beta-Hemolytic Streptococcus	145 835
Beta-1-C Fraction	278
Beta 2-Glycoprotein	121

Substance Analyzed	Reference Number
Bilharziasis	555
Biologically Active Hormone	166
Blastokinin	728
Blastokinin Amino Acid Composition	606
Blood Coagulation Factors	37
Blood Donor Screening	357
Blood Lymphocyte Fractions	616
Blood Platelets	466
B Cells	677
Blood Plasma and Lymph	178
Blood Proteins	127A 247 248 249
Blood Serum Albumin	366
Blood Stains	1047
Bone Marrow Cells	678
Bovine Allantoic Fluid	165
Bovine Corneal Epithelium	130
Bovine Milk Caseins	1024
Bovine Serum Proteins	139
Brain Acetylcholinesterase	954
Brain Myelin	658
Brain Proteins	17 928 952 428
Brucella Sonic Extract	326
Brucella Species	325
Bull Semen Plasma	425
Candida	796

Substance Analyzed	Reference Number
Candida Albicans	875 1056
Candida Antigens	945
Carbohydrate Half Sulphate Esters	671
Carbohydrate Protein	631
Carbonic Anhydrase Isozymes	1089
Carnitine Palmitoyltransferase	288
Carrier Ampholytes	850
Carrier Proteins	446
Cell Electrophoresis	745
Cell Organelles	895
Cell Proteins	693
Cellular Antigens in Myxo- and Paramyxoviruses	505
Cellular Blood Elements	423
Cellular Electrophoreis	71
Cellular RNA	908
Cerebrospinal Fluid	176 629
Cerebrospinal Fluid Proteins	893 1000A
Cervical Mucus	630
Chicken Serum	86
Chad Herbivora	449
Cholera	147
Cholestasis	395
Cholinesterases	1051
Chorionic Somatomammotropin	985
Chromogrannine	697
Chromophoric Amino Acid	648
Circulating Blood	75
Circulating DNA	931

Substance Analyzed	Reference Number
Cirrhosis	107
Clostridium Botulinum Type A Toxin	453
Coat Proteins	1076
Colostrum Immunoglobulins	554
C-Reactive Protein	491
C-Reactive Protein in Tuberculous	722
C 3 Polymorphism	459
Cutaneous Manifestations of Allergy	303
Cysticercosis	252
Cytochrome 553	168
Cytochrome C	515
Cytoplasmic and Mitochondrial Aconitate Hydratases	869
Definition of a Method of Histobiochemical Analysis	266
Deoxyribonucleic Acid Base Composition	542
Dermal Acid Mucopolysaccharides	1041
Determination of the Size of Viruses using Gel Electrophoresis	258
D Group Streptococci Sera	59
Diagnosis of Bilharziasis	60
Diagnosis of Meningococcal Infections	171
Diagnosis of Parasitoses	57
Diagnosis of Tay-Sachs Disease	588
Diagnostic Significance of Electrophoresis	62
Dioxygenase, Querecentinase	270
Dissociated Cells P-Benzoquinone, Tannic Acid	475
DNA Polymerase	64
Double Pre-Beta Bands	287
Dysproteinemia in Liver Cirrhosis	124
Ehrlich Ascites	64
Electrophoresis of Drugs	604
Electrophoretic Analysis of Cell Populations in Presumptive Epidermis	336

Substance Analyzed	Reference Number
Electrophoretic Extraction	173
Electrophoretic Separation of Lymphocytes	779
11S Globulin Soybean Seeds	1042
Embryo Specific Alpha-Globulins	529
Encephalitis Virus	213
Encephalitogenic Protein	798
Cell Proteins of T-Strain Mycoplasmas	497
Encephalomyelitis	371
Enterotoxin Clostridium Perfringens Type A	759
Envelope Proteins	191
Enzyme	473 611
Enzyme Electrophoretograms	97
Enzyme Typing of Bloodstains	108
Epidemic Parotitis	249
Equine Growth Hormone	932
Erythrocyte	582
Erythrocyte Acid Phosphatase	79
Erythrocyte Carbonic Anhydrases	198
Erythrocyte Peptidases	101
Escherichia Coli Exotoxin	362
Escherichia Coli K12 Soluble Proteins	128
Ewing's Sarcoma	78
Exoantigen	223
Fatty Acids	743 989
Ferric Myoglobin	964
Ferritin	651 714 715 716 944

Substance Analyzed	Reference Number
Fibrinogen	781 993
Fibrinolytic	916
Fibrinopeptides	506
Five Main Histone Fractions	363
Foetal Hemoglobin	299
Follicle-Stimulating and Luteinizing Hormones	520
4S Antigens	680
Fowlpox and Vaccinia Virus Proteins	940
Fowl Spermatozoa	318
Fractional Methods	268
Fractionation of Proteins	237
Fructose-6-Phosphate Phosphoketolase	177
FSH in Swine	106
Galactose-1-Phosphate Uridyl Transferase	142
Galanthamine	624
Gamma-Globulins	151 307
Gammopathies	408
Gangliosides	730
GC Component in Human Serum	55
GC Types	212
Gene-Frequency	459
Generic Identification of L-Forms	149
Genetically Different Proteins	530
Globin	994
Globulin	339 877
Glomerulonephritis	278
Glucose Metabolites	1071 1072
Glucose-6-Phosphate Dehydrogenase	749

Substance Analyzed	Reference Number
Glucose-6-Phosphate Dehydrogenase Isoenzymes	30
Glucuronidase	739
Glyceraldehyde-3-Phosphate Dehydrogenase, Fructoaldolase, Glyoxalase II and Sorbitol Dehydrogenase	1116
Glycoprotein Hormones	795
Glycoproteins	132 185 247 248 249 335 774
Glycosidases	633
GOT Isoenzyme	136
Grain Proteins	846
Haemoglobin	105 575 732
Haemoglobin Electrophoresis	186
Haemoglobin Malmo	575
Halophilic Enzyme	528
Haptoglobins	1048
HCG	183
Heat-Labile Toxin of Bordetella Pertussis	102
Hela Cell Metaphase Chromosomes	664
Hemoglobin	32 515
Hemoglobin A2	241 513
Hemoglobin-Binding Protein	480
Hemoglobin Octamer	15
Hemoglobinopathies	757
Hemoglobin S	1027 1018A
Hemoglobin Solutions	369

Substance Analyzed	Reference Number
Hemophilus Infleunzae Type B	998
Heparin and Protamine Sulfate	9
Hepatic Phosphoenolpyruvate Carboxykinase	934
Hepatitis	273
Hepatitis-Associated Antigen	174 182 297 359 277
Hepatitis-Homologous	358
Herpes Simplex Virus	744
Hexokinase in Cell Homogenates from Baker's Yeast	251
Histidine-Binding Protein J	620
Histidine Transport	620
Histones	1060
Histoplasma Capsulata Practical Diagnostic Results	261
Horseradish Peroxidase	800
H 3-RNA	1010
Human Alpha-2 Lipoprotein Bands	126
Human and Animal Hemoglobins	328
Human Anti-CEA	1131
Human Blood Platelets	552
Human Chorionic Gonadotropin	479
Human Chorionic Gonadotropin Luteinizing Hormone	782
Human Chorionic Somatomammotropin	985
Human Erythrocuprein	8
Human Erythrocytes	655
Human Follicle Stimulating Hormone	986
Human Haptoglobin 1-1 Molecule	116
Human Hemoglobins	152
Human Liver Alkaline Phosphatase	445
Human Lymphocytes	71 282 348

Substance Analyzed	Reference Number
Hydroxyindole-O-Methyltransferase	206
Hyperlipoproteinaemia	760
Hyperlipoproteinemias	232 429
Hypoxanthine-Guanine Phosphoribosyl Transferase	67
IBR-Virus	1025
Identification of Antibiotics	82
IGG I, II, and III	332
IGG-Paraproteinemias	38
IGM-Fraction	170
Immune Globulins with Antitoxic Activity	77
Immunoelectrophoresis in Forensic Medicine	162
Immunoelectrophoretic	411
Immunoglobulin Analysis	150
Immunoglobulins	936 1044
Immunoglobulins G	332
Immunorheophoresis	119
Lactate Dehydrogenase	462 485 486 851
Lactogenic Factor	413
Lactoglobulin	1043
Lamb Fetuin	886
L-Arginase	729
L-Asparaginase	823
L-Cell Interferons	199
LDH-Isoenzymes	110 949
Leishmaniasis	519
Leucosis	72
Leukemia	264
Leukocyte Alkaline Phosphatase	340
L-Forms and Mycoplasma	309

Substance Analyzed	Reference Number
Membrane Enzymes	12
Membranous Proteins	474
Meningococcal Arthritis	876
Mercaptalbumin, and Beta-Lactoglobulins A and B	403
Metallothionein	1125
Microbial Electrophoresis	534
Mycoplasma Mycoides	874
Myosin	279 853
N-Acetyl-D-Hexosaminamidase Isoenzymes	588
Neuraminidase	636 833
Neurospecific S-100 Protein Fractions	179
Nitrogen Compounds in Body Fluids	330
Nonhistone Chromosomal Proteins	783
Nonspecific Esterases in Blood Serum	65
Normal Human Lymphocyte	255
Normal Sera	46
Nucleic Acid	81 723
Nucleic Acid Bases	537
Nucleolar Proteins	892
Nucleosides Purines Pyrimidines	753
Numerous Samples Simultaneously	250
Microheterogeneity of Fetuin	184
Mitochondria	288
Monoclonal Gammopathies	262
Monospecific Antibody to Human Sulfatase	230
Motility	318
M-Proteins	274
Mucin Glycoproteins	774
Mucopolysaccharides	129 905
Multiple Molecular Forms	427

Substance Analyzed	Reference Number
Muscle Proteins	220
	233
	853
Muscular Parvalbumins	167
Mycobacteria	245
	980
Mycobacterial Antigens	1022
	1053
	990
Mycobacterium Tuberculosis	788
Mycoplasma	884
Oligo Globulin	469
Oligonucleotide Isopliths	95
Oncogenic Ribonucleic Acid Viruses	814
Ophiobolus Graminis Sacc	457
Organelles	195
Ovomucoid Heterogeneity	256
Paracoccidioidomycosis	926
Parameters of Thyroid Function in Serum	33
Paraproteinaemia	226
	659
Paraproteins	89
	569
	436
Paraproteinemias	123
Paraprotein Diseases	296
Paraproteins of Serum	272
Parotid Secretion	42
Partial Isolation of Human Renin	386
Pasteurella Pestis	148
Pathological Lymph Nodes	122
Penicillium Conidia	300

Substance Analyzed	Reference Number
Pepsinogen and Pepsin Fractions	432
Peptide Mixtures	164A
Periodontal Diseases	157
Peripheral Blood Lymphocytes	521
Peripheral Lymphocytes	122
Peromyscus 7S 1 Globulins	643
Peroxidases	683
Peroxidase Isozymes	684
Phenotyping of Hyperlipoproteinemias	94
Phialophora Verrucosa, Fonsecaea Pedrosoi and Cladosporium Carrioni	440
Phlebotomus Group of Arboviruses	546
Phosphoacetylglucosamine Mutase	239
Phosphoglucomutase Types	472
Phosphoglycerate Kinase	751
Phospholipid	76
Phythohaemagglutinin	450 1102
Pituitary Gonadotropins	382
Pituitary Prolactin	925
Plant Viral Protein	501
Plant Viral RNA Plasma Albumin	403
Plasma and Urinary Amino Acids	20
Plasmacytoma	305
Plasma Hyperbetalipoproteinemia	679
Plasma Kinen-Forming System	857
Plasma Lipoproteins	260 293 484
Plasma Prekallikrein	825
Plasma Proteins	44 995
Pneumococcal Bacteraemia	367
Poliovirus Antigens	201

Substance Analyzed	Reference Number
Poliovirus Inhibitors	200
Polyacrylamide	683
Polyglycine	439
Polymorphous Enzymes Glutamate Pyruvate Transaminase and Phosphoglucomutase	603
Polypeptides of Influenza Virus	500
Polysaccharides	405
Post-Albumin Proteins	66
Prealbumin	735
Pre-Beta Lipoprotein	397 709
Preformed Antibody	173
Pregnancy-Specific Protein	334
Primary Cancer of the Liver	138
Primary Hyperlipidemia	627
Progesterone Binding Protein (PBP)	997
Prolactin	893 985
Prolongation of Heterograft	173
Protein and LDH-Isoenzyme	641
Proteinase	1115
Protein Composition	470
Protein Detection and Isolation	109
Protein Fractions	414 516
Protein, Myogen and Myosin	220
Protein Polymers	148
Protein Polymorphism	112
Protein Quantitation	292
Protein Separations	286
Proteins	1073 125 135 905 909 923 980

Substance Analyzed	Reference Number
Proteins (continued)	463 511 512 647
Proteins and Carbohydrates	236
Proteins and Nuclear Acids	847
Proteins Extracted from Subcellular Structures of Brain	50
Proteins from Carrier Ampholytes	533
Influenza Virus	636
Insoluble Brain Proteins	1061
Insulin	493 988
Interacting Protein Systems	848
Interferons	536 790
Intestinal Mucosal Epithelial Cell	147
Investigation of Protein Drugs	591
IPV-Virus	1025
Isocitrate Dehydrogenase	935
Isoelectric Fractionation in Protein	240
Isoelectric Separation of Proteins	391
Isoenzyme Fructosephosphate Aldolase	96
Isoenzymes	1070
Isolation, Characterization of Two Phospholipase A's	228
Isolation of Blood Cells	721
Isomeric Chondroitin Sulfates	510
Jack Bean Proteins	706
Jack Bean Urease	807
Proteins in Serum	291
Proteins of Parainfluenza Virus SV5	100
Protein-Sodium Dodecyl Sulfate Complexes	576
Protein Synthesis by Lymphocytes	460

Substance Analyzed	Reference Number
Proteinuria	280
Proteolytic Enzymes	461
Pseudomonas Aeruginosa Haemolysin	337
Pseudoparaproteinemia	442
Psoriatic Epidermis	426
Pulmonary Aspergillosis	360
Pulmonary Edematous Fluid	921
Purified Allergens	354
Purines and Pyrimidines	753
Pyruvate Kinase	1033
Rabbit Antisera	76
Radicular Cysts and Granulomas	929
Rat Brain Proteins	889
Rat Liver Chromatin	726
Rat Liver Decarboxylases	117
Rat Liver Lysosomes	195
Rat Serum Lipoproteins	243
Recovery of Protein	590
Red Cell Enzyme Polymorphisms	563
Renin	553
Reverse Transcriptase	1020
Rheumatic Diseases	799
Rheumatism	155
Ribonuclease	1054
Ribonuclease Inhibitor	544
Ribonucleic Acid	255 1039 1128
Ribosomal Proteins	688 851
Ribulose-1, 5-Diphosphate	1119
RNA	329 978 1009

Substance Analyzed	Reference Number
RNA-Rich Fraction	840
Sarcoplasmic and Mitochondrial Isoenzymes	49
Schistosoma Mansoni Alpha-Naphthyl Acetate Esterases	131
Scand J Clin Lab Invest 29, Suppl, 1972	584
Schistosomiasis	61
Securinin	624
Seminoprotein (-SM)	612
Separated Proteins	45
Separation of Proteins in Concentrated Cerebrospinal Fluid	285
Seric Proteins	238
Serum Aklaline Phosphatases	163
Serum Beta and Pre-Beta-Lipoproteins	271
Serum Beta Lipoproteins	70
Serum Glycoproteins	21 26
Serum Hepatitis	276
Serum Lipoprotein Analysis	.437
Serum Lipoproteins	507 523
Serum Lipoprotein Patterns	134
Separation of Lymphocytes	737
Serum	708
Serum Immunoglobulins	992
Serum LDH Isoenzyme	752
Serum Protein Fractions	24
Serum Protein Electrophoresis	374
Serum Protein	1045 1050 820 801 733 668 667 656 632

Substance Analyzed	Reference Number
Serum Protein (continued)	563
	495
	494
	410
	333
	303
	180
	157
	156
	140
	127
	107
	43
	36
	11
Serum Lipoproteins	742
	666
	346
	275
	232
	114
Serum Proteins Electrophoresis in Liver Diseases	396
Serum Proteins in Leprosy	141
Serum Lipoproteins	267
Sheep Serum	103
16 Different Blood Proteins	489
Single Components in Protein Mixtures	202
Sickleanemia	186
Sickledex	804
Skin Test Antigen SST	39
Soluble Extracts of Dirofilaria Immitis	210
Soluble Liver Proteins	820
Soluble Proteins	999
Some Proteins	269
Sonicated Human Serum Proteins	41
Sow Milk	991
Specific Enzyme of Human Sperm	338
Sperm in Sperm Stains	153

Substance Analyzed	Reference Number
Spinal Fluid	892 1001
Staphylococcal Enterotoxin	900
Staphylococcal Enterotoxin C2	758
Staphyloccus Aureus Extracts	1098
S-Sulfo Derivatives of Fibrinogen	29
Staphylococcal Toxins	40
Streptococcus Mutans	53
Streptolysin	836
Study of Liver Disease	357
Sulfated Nucleotides	420
Sulphur-Rich Proteins from Wool	578
Surface Antibodies	71
Synovia	188
Synovial Proteins	301
T and B Lymphocytes	677
Tears	482
T4 Genes 44 and 62	1094
Thalassaemia Syndromes	105
Thalassemia	25
32 P-Labeled RNA	1066
3,5,3-L-Tri-Iodothyronine-Binding, Proteins	483
Thrombocytic Properties	217
Thymus Specific Antigen	1085
Thyroid Diseases	809
Thyroid Follicles	1073
Thyroid Hormone	447 735
Thyroxine-Binding	883
Thyroxine-Binding Human Serum Proteins	133
Thyroxine-Binding Protein	458
Timothy Pollen Antigen	298
Tissue and Serum Creatine Kinase Isoenzymes	598

Substance Analyzed	Reference Number
208 TL and 207 TL	644
Tobacco Rattle Virus Protein	939
Toxicosis	339
Toxoplasma Gondii	518
Treponemal Antigen	640
Triiodothyronine-TBPA	735
Triprotamines	164
Trypanosoma Brucei	223
Trypanosoma Cruzi	51
Tryptophanyl Transfer RNA Synthetase from Lymphocytes	264
2M, IGA and IGM	962
Urinary Amino Acids	22
Urinary Delta-Aminolevulinic Acid	488
Urinary Proteins	448
Uranyl-Resistant Paraproteins	409
Vaccinia Antigen and Antibody	885
Viral Hepatitis	21
Virus	13
Viruses of Vaccinia, Buffalopox, Variola and Alastrim	548
Virus Particles Type C and A	725
Vitamin B 12-Binding Substances	175
Water-Soluble Proteins	157A
Weber-Edsall Extract and Actomyosin	347
S-(4-Pyridylethyl)-L-Cysteine Myosin	736
SH Antigen	357

APPENDIX 5

RESPONSE OF THE SCIENTIFIC COMMUNITY

Letters of inquiry were sent to the following members of the sceintific community:

Dr. Eugene A. Arnold
Department of Pathology
Johns Hopkins University School of Medicine

Dr. J. Austin
Divisions of Neurology and Clinical Immunology
University of Colorado Medical Center

Dr. Barbara-Anne Battelle
Biology Department
Syracuse University

Dr. P. J. Bechtel
Department of Food Science and Human Nutrition
Michigan State University

Dr. H. N. Bhargava
Department of Pharmacology
University of California School of Medicine

Dr. C. E. Bodwell
Protein Nutrition Laboratory
Human Nutrition Research Division
Agricultural Research Service
United States Department of Agriculture

Dr. James Bonner
Division of Biology
California Institute of Technology

Dr. Rosaria P. Brivio
Biology Department
Syracuse University

Dr. N. Catsimpoolas
Laboratory of Protein Chemistry
Central Soya Research Center

Dr. S. L. Chan
Department of Pharmacology
University of California School of Medicine

Ms. Rosalyn Cleevey
The Home Office Central Research Establishment
Aldermaston
Berkshire, England

Ms. Mary Davies
The Home Office Central Research Establishment
Aldermaston
Berkshire, England

Dr. Paul J. Davis
Department of Medicine
Baltimore City Hospital

Dr. S. Dasqupta
Department of Biology
Saint Louis University

Dr. Friedrick Deinhardt
Department of Microbiology
Rush-Presbyterian-St. Lukes Medical Center

Dr. R. De Wachter
Laboratory of Physiological Chemistry
State University of Ghent
Ghent, Belgium

Dr. John T. Dulaney
Department of Molecular Biology
Vanderbilt University

Dr. Sarah C. R. Elgin
Division of Biology
California Institute of Technology

Dr. E. J. Field
Demyelinating Diseases Unit
Newcastle General Hospital
Newcastle-upon-Tyne, England

Dr. James R. Florini
Biology Department
Syracuse University

Dr. E. Gardner
Department of Pharmacology
University of California School of Medicine

Dr. Robert A. Good
Department of Pathology
University of Minnesota

Dr. Robert I. Gregerman
Gerontology Research Center
National Institute of Child Health and Human Development
National Institute of Health

Dr. A. L. Griffith
Department of Anatomy
University of Illinois at the Medical Center

Dr. E. A. Grula
Department of Microbiology
Oklahoma State University

Dr. Barry S. Handwerger
Department of Medicine
Johns Hopkins University School of Medicine

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Max-Planck-Institut für Eiweiss und Lederforschung
8 Müchen
West Germany

Dr. John Hoekstra
Department of Microbiology
Rush-Presbyterian-St. Lukes Medical Center

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University of Cambridge
Cambridge CB2 1QW, United Kingdom

Dr. B. M. Jones
University College of Wales
Department of Zoology
Aberystwth, Wales

Dr. Paul Kaesberg
Biophysics Laboratory and Department of Biochemistry
University of Wisconsin

Dr. R. B. Kemp
Department of Zoology
University College of Wales
Aberystwth, Wales

Dr. S. S. Kind
Forensic Science Laboratory
Government Buildings
Broadway West
Gasforth
Newcastle-upon-Tyne, England

Dr. P. Kohler
Divisions of Neurology and Clinical Immunology
University of Colorado Medical Center

Dr. Arthur La Velle
Department of Anatomy
University of Illinois at the Medical Center

Dr. Gary W. Litman
Department of Pathology
University of Minnesota

Dr. K. P. Maier
Medizinische Universitäts
78 Freiburg
West Germany

Dr. David C. Merz
Department of Pathology
University of Minnesota

Ms. Patricia A. Morris
Home Office Central Research Establishment
Aldermaston
Berkshire, England

Dr. Neuwelt
Divisions of Neurology and Clinical Immunology
University of Colorado Medical Center

Dr. Gunner F. Nordberg
Department of Hygiene
Karolinska Institute
Stockholm, Sweden

Dr. Monica Nordberg
Department of Hygiene
Karolinska Institute
Stockholm, Sweden

Dr. Constance Molino Park
Albert Einstein College of Medicine

Dr. A. M. Pearson
Department of Food Science and Human Nutrition
Michigan State University

Dr. Magnus Piscator
Department of Hygiene
Karolinska Institute
Stockholm, Sweden

Mr. A. Plough
Plough Incorporated

Dr. C. F. Savory
Department of Microbiology
Oklahoma State University

Dr. D. Y. Schirachi
Department of Pharmacology
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California Institute of Technology

Dr. D. Stumpee
Divisions of Neurology and Clinical Immunology
University of Colorado Medical Center

Dr. Oscar Touster
Department of Molecular Biology
Vanderbilt University

Dr. A. J. Trevor
Department of Pharmacology
University of California School of Medicine

Dr. Olof Vesterberg
National Institute of Occupational Health
S-104 01
Stockholm 60, Sweden

Dr. O. Vesterberg
Chemistry Department
National Institute
S-104 01
Stockholm 60, Sweden

Dr. P. H. Whitehead
Metropolitan Police Forensic Science Laboratory
Holborn
London WV, England

Dr. Takaski Yamada
National Cancer Research Institute
Division of Pathology
Tokyo, Japan

Dr. Keith E. Young
Department of Pathology
Johns Hopkins University School of Medicine

UNIVERSITEIT ANTWERPEN

UNIVERSITAIRE INSTELLING ANTWERPEN

Dept. Celbiologie
O. Ref. RDW/VH 740263

Mrs. P.A. Gempel
Chemical Systems Section
Arthur D. Little, Inc.
Acorn Park
Cambridge
Massachusetts 02140 .(617)864-5770

Wilrijk, June 6, 1974.

Dear Mrs. Gempel,

I must first of all apologize for replying so late to your letter, dated april 19th, in which you ask me if I see any advantage in application of electrophoretic techniques in zero g surroundings. This is due to the fact that my address has changed and I only received your letter with much delay.

I am sorry to disappoint you, but although it may be true that electrophoresis carried out in space may not have some of the drawbacks of the technique as carried out on the surface of the earth, I would consider that it is not worthwhile investing in research on this subject at the moment.

I am convinced that spaceflight is a very far-reaching achievement, but that it can be better used for other and more important purposes than the improvement of separation techniques.

Sincerely yours,

Dr. R. De Wachter
Department of cell biology.

UNIVERSITEITSPLEIN 1 — 2610 WILRIJK — TEL. 03/28.25.28

CALIFORNIA INSTITUTE OF TECHNOLOGY

PASADENA, CALIFORNIA 91109

DIVISION OF BIOLOGY

May 20, 1974

Ms. Patricia Gempel:
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Ms. Patricia Gempel:

In reply to your letter of April 19, 1974, I do not feel at this time that the electrophoretic separation of viral proteins, or whole virus particles in space at zero gravity would be a feasible project. Although such an experiment would be interesting in a theoretical sense, the increased resolution would probably not justify the expense involved. Moreover, most biological procedures (unlike certain experiments in physics or astronomy) need to be available on a routine basis in order to be valuable to the research worker.

I have also sent a copy of this letter to Dr. Paul Kaesberg, who is still working with bacterial viruses, and with Qβ in particular. I am no longer working with this type of virus. The Group A arbovirus which I am currently using is too large for this approach.

I thank you for your interest; however, for the reasons listed above I am not interested in collaboration at this time.

Sincerely yours,

Ellen G. Strauss

Ellen G. Strauss

EGS:rt
cc: Dr. Paul Kaesberg

SYRACUSE UNIVERSITY

DEPARTMENT OF BIOLOGY | 209 LYMAN HALL

108 COLLEGE PLACE | SYRACUSE, NEW YORK 13210
TELEPHONE 315 | 423-2821

April 26, 1974

Dr. Patricia A. Gempel
Chemical Systems Section
Arthur D. Little, Inc.
Acorn Park
Cambridge, Mass. 02140

Dear Dr. Gempel:

Your letter has caused me a crisis of conscience. As a long time aviation-space fan (I built model airplanes as a boy, and now I am a Flight Instructor with about 850 hours flight time), the prospect of doing anything even remotely associated with the Skylab system is very appealing, and I am greatly tempted to bend my scientific judgement on this matter.

However, try as I might - and I certainly do - I cannot find persuasive advantages for analyses of myosin by isoelectric focusing under zero gravity. In part, this may be because I have never thought of this aspect of things. Even such an elementary and obvious point as the effects on convection did not occur to me until you raised it in your letter, so there may be other factors I have not considered. Frankly, I hope so - I would be delighted if you could persuade me that some of our samples should be analyzed at zero gravity.

There is one other snag, however. Now that Drs. Brivio and Battelle have left my lab, we are not doing IEF of myosin any longer. If you are interested only in having a myosin sample to try, there are many people (some of them in Boston) better qualified than I to furnish it. And Barbara Battelle is currently on a post-doc in Sidman's lab at Harvard Medical, so she is conveniently nearby if you want to talk with her.

On the other hand, if you feel that my lab may be able to make some contributions to the zero gravity approach, I would be delighted to have you attempt to persuade me. My phone is AC315, 423-2510.

Sincerely yours,

James R. Florini

James R. Florini, Ph.D.
Professor of Biochemistry

JRF:ef

CITY OF BALTIMORE
WILLIAM DONALD SCHAEFER, Mayor

DEPARTMENT OF HOSPITALS
FREDERIC C. HUBBARD, Director
1240 Eastern Avenue, Baltimore, Maryland 21224

April 26, 1974

Ms. Patricia A. Gempel
Chemical Systems Section
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Ms. Gempel:

I am writing in reply to your letter of April 19, in which you suggested that an electrophoresis system we described several years ago might have improved resolution of proteins in a "zero g" atmosphere. As you probably know, the technique we reported (J Clin Endocrinol Metab 30:237, 1970; ibid., 33:699, 1971; J Clin Invest 51:515, 1972) depends upon the buffers developed by N.E. Good (Biochemistry 5:467, 1966); such buffers were constructed for use in the "physiologic pH range," and indeed have proved to be quite satisfactory electrophoresis buffers. Andreas Chrambach at NIH has written about the use of these buffers in several long papers. As you no doubt noted from the reading of the JCI paper, the electrophoresis system we used was a continuous one.

While the pH 7.4 method was satisfactory for resolving the three thyroid hormone-binding proteins in human serum, it is poor at protein resolution in general. The method can be improved by introducing some discontinuities (of pore size, molarity), but we have insisted on homogeneous pH. Protein-protein interactions may be more prominent at pH 7.4, impeding resolution. We are now investigating the electrophoretic characteristics of soluble intracellular proteins which bind thyroid hormones and are interested in improved resolution of such proteins at physiologic pH. (Such soluble proteins focus as three peaks on isoelectric fractionation, but we have been able to demonstrate only one moiety in various polyacrylamide gel electrophoresis systems; it is unclear whether the isoelectric focusing studies represent a phenomenon of buffer ampholyte interaction with one protein or whether there are in fact more than one binding protein in cytoplasm.)

In any event, I would be interested in talking at the issue of improving resolution in the physiologic pH electrophoresis systems. My telephone number here is 342-5400, extension 1331 (area code 301).

I appreciate your interest.

Sincerely,

Paul J. Davis, M.D., Head
Endocrinology Division

Associate Professor of Medicine
Johns Hopkins University

PJD:chm

CALIFORNIA INSTITUTE OF TECHNOLOGY

PASADENA, CALIFORNIA 91109

DIVISION OF BIOLOGY

April 30, 1974

Dr. Patricia A. Gempel
Chemical Systems Section
Arthur D. Little, Inc.
Acorn Park
Cambridge, Massachusetts 02140

Dear Dr. Gempel:

As you have no doubt learned, Dr. Sarah Elgin is now Professor Sarah Elgin, Dept. of Biochemistry and Molecular Biology, Harvard University. Write her there.

Yours,

James Bonner
Professor of Biology

JB:ds

NEWCASTLE UNIVERSITY HOSPITALS
NEWCASTLE GENERAL HOSPITAL
WESTGATE ROAD NEWCASTLE UPON TYNE NE4 6BE

DEPARTMENT OF PATHOLOGY

PROFESSOR B. E. TOMLINSON
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Dr. T. BIRD
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Dr. R. O. K. SCHADE
Dr. J. B. SELKON
Dr. A. R. MORLEY

TELEPHONE
NEWCASTLE 38811
STD 0632

9th May, 1974.

Mrs. Patricia A. Gempel,
Chemical Systems Section,
Arthur D. Little, Inc.,
Acorn Park,
CAMBRIDGE,
Massachusetts,
U.S.A.

Dear Mrs. Gempel, Thankyou for your letter of April 22nd (/ks)

Certainly a "zero g" environment would be helpful in overcoming some of the difficulties in making measurement. Drift (thermal or mechanical) as well as sedimentation would be eliminated, and this would much alleviate the tax on the patience of the observer.

But, frankly, I do not see how one is going to look down a microscope and "time" cells in a "zero g" environment. Or have you ingeniously catered for this? I would be most interested to hear.

Yours sincerely,

E. J. Field
Professor of Experimental Neuropathology

Home Office
CENTRAL RESEARCH ESTABLISHMENT
Aldermaston Reading Berkshire RG7 4PN

Telephone Tadley 3833 (STD Code 0735 6) extension 5853
Director A S Curry MA PhD FRIC FRCPath

Dr Patricia A Gempel
Chemical Systems Section
Arthur D Little Inc
Acorn Park
Cambridge Mass 02140
USA

Please reply to The Director
Your reference

Our reference CRE/PHW

Date 8 May 1974

Dear Dr Gempel

Thank you for your recent letter concerning electrophoresis in a "zero g" atmosphere.

While we have considerable experience in electrophoresis of red cell enzymes and serum proteins using most of the conventional media (and more recently iso-electric focusing), the prospect of carrying out experiments in a zero-gravity atmosphere is one that, I confess, had not crossed my mind.

I regret I am not familiar with work carried on under such conditions but would be interested to hear of any results. It may be that if "zero g" conditions are easily obtained in the laboratory and greater resolution is obtained of enzyme variants, for example, then it may be interesting for us to investigate.

I would be interested to hear further of your work and discuss the possible forensic implications, if any, with you or your people.

I understand you have an office in London - perhaps I could have a chat with someone there?

I look forward to hearing from you.

Yours sincerely

Patrick H. Whitehead

Dr P H Whitehead

MICHIGAN STATE UNIVERSITY

DEPARTMENT OF FOOD SCIENCE AND HUMAN NUTRITION EAST LANSING • MICHIGAN • 48824

May 10, 1974

Ms. Patricia A. Gempel
Chemical Systems Section
Arthur D. Little, Inc.
Acorn Park
Cambridge, MA 02140

Dear Ms. Gempel:

Thank you for your letter of April 19 to Dr. P. J. Bechtel, who is now working with Dr. E. G. Krebs in the Medical School at the University of California in Davis. In his absence, I am replying to your letter.

I would be very pleased to visit with you further on the possibility of increasing the solubility of proteins by working at zero gravity. The procedure certainly sounds interesting, and I would be happy to talk to you more concerning it. If you should be able to visit us on campus, Dr. J. R. Brunner of this Department who is well versed in electrophoretic techniques would also like to visit with you.

Will look forward to hearing from you.

Sincerely yours,

A. M. Pearson, Professor
Food Science & Human Nutrition

AMP/lk

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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SANTA BARBARA • SANTA CRUZ

SCHOOL OF MEDICINE
DEPARTMENT OF PHARMACOLOGY

SAN FRANCISCO, CALIFORNIA 94143

April 29, 1974

Ms. Patricia A. Gempel
Chemical Systems Section
Arthur D. Little, Inc.
Cambridge, Mass. 02140

Dear Ms. Gempel:

I have read your letter with considerable interest although with some puzzlement. It would be nice to know in somewhat more detail the nature of your deliberations. At this moment it is difficult for me to visualize any particular advantage to be derived from performing electrophresis in a "zero g" environment. This is a technique with which I have had considerable experience and your implications have piqued my curiosity.

The article which you refer to on "Purification and..." relies mainly on liquid chromatography, a technique which depends largely on gravitational forces for its success. In two subsequent publications the use of electrophretic techniques are described in somewhat more detail.

Needless to say I would be interested in the opportunity to explore this subject further with you.

Cordially,

Eugene Gardner

Eugene Gardner, Ph.D.

THE UNIVERSITY COLLEGE OF WALES
DEPARTMENT OF ZOOLOGY

Telephone : 3111

PENGLAIS
ABERYSTWYTH
SY23 3DA

PROFESSOR BRYN M. JONES

17th June 1974

Miss P.A. Gempel,
Chemical Systems Section,
Arthur D. Little Inc.,
Acorn Park,
Cambridge, Massachusetts 02140.

Dear Miss Gempel,

I am sorry for the delay in replying to your letter of 22nd April 1974 but I was absent from Aberystwyth for a considerable period of time. I can see the value of "Zero-G" for electrophoretic separation especially of heavy particles for instance cells in suspension. In fact, I discussed with Bier his attempted experiment in one of the Appollo Spacecrafts.

You are perhaps right in thinking that aggregation might be decreased in "Zero-G" conditions but I have no idea how "Zero-G" might affect the Physiochemical parameters (Vander Waal's forces, electrostatics etc.) responsible for adhesion, the mechanism of cell aggregation. Of course, cells have to make contact to adhere and "Zero-G" would affect this. It might also affect the movement of cells within an aggregate or their movement on artificial surfaces, dependent upon production of cellular processes (altered by "Zero-G"?). In fact the general question of the effect of such conditions on the ultrastructure of cells in culture might be worth considering.

I would certainly be interested in considering this possibility with you.

Yours sincerely,

Dr. R.B. Kemp.

NATIONAL BOARD OF OCCUPATIONAL
SAFETY AND HEALTH
Department of Occupational Health

Chemical Division
Associate Professor Olof Vesterberg, LE

1974-05-29

Dr. Patricia A. Gempel
Arthur D. Little, Inc.
Acorn Park
Cambridge Mass. 02140
USA

Dear Dr. Gempel,

This is a reply to your letter of April 19, 1974. Without question you raise an interesting approach to electrophoretic procedures. I have been working with isoelectric focusing for more than 10 years. In ~~t~~three technique convection as well as sedimentation has to be counteracted by one means or another. Earlier density gradients or gels such as polyacrylamide have been used for this purpose, however, these solutions are not ideal and there exist really a need for a means were these agents can be avoided. Other reason for this is that they might interfere with the determination of isoelectric points of protein. As you might know isoelectric focusing is very unique, because it makes possible the determination of isoelectric points (pI) of proteins in the simple way. Isoelectric points determined in this way are very valuable physico-chemical constant of proteins of an importance that can be compared with molecular weight data. The reason why these pI values have not yet become into more general use is that they can be influenced by various factors, e.g. ionic strength when determined by older technique such as electrophoresis, but they seem to be determinable with the high degree of reproducibility by isoelectro focusing.

For the reasons mentioned above I would be very interested in discussing with you the possibility to performe focusing in zero gravity atmosphere as you propose in your letter. For your information I can give you references to other articles on isoelectric focusing that are of more general value than the one you mentioned in your letter. I send you some copies of reprints and would be glad to supply you with more references also from other authors in forthcoming letters.

Yours sincerely,

231

Olof Vesterberg

Encl.

Mailing address
Fack

Telephone no
08 - 23 69 00

Telegrams
Occuphealth

APPENDIX 6

SURVEY OF DIAGNOSTIC LABORATORY TESTS

1. Rubella Antibody Detection

Methods:

Hemmagglutination inhibition (HI)
Complement fixation (CF)
Indirect fluorescent antibody
Neutralization tests (takes 7-11 days)

Clinical Use:

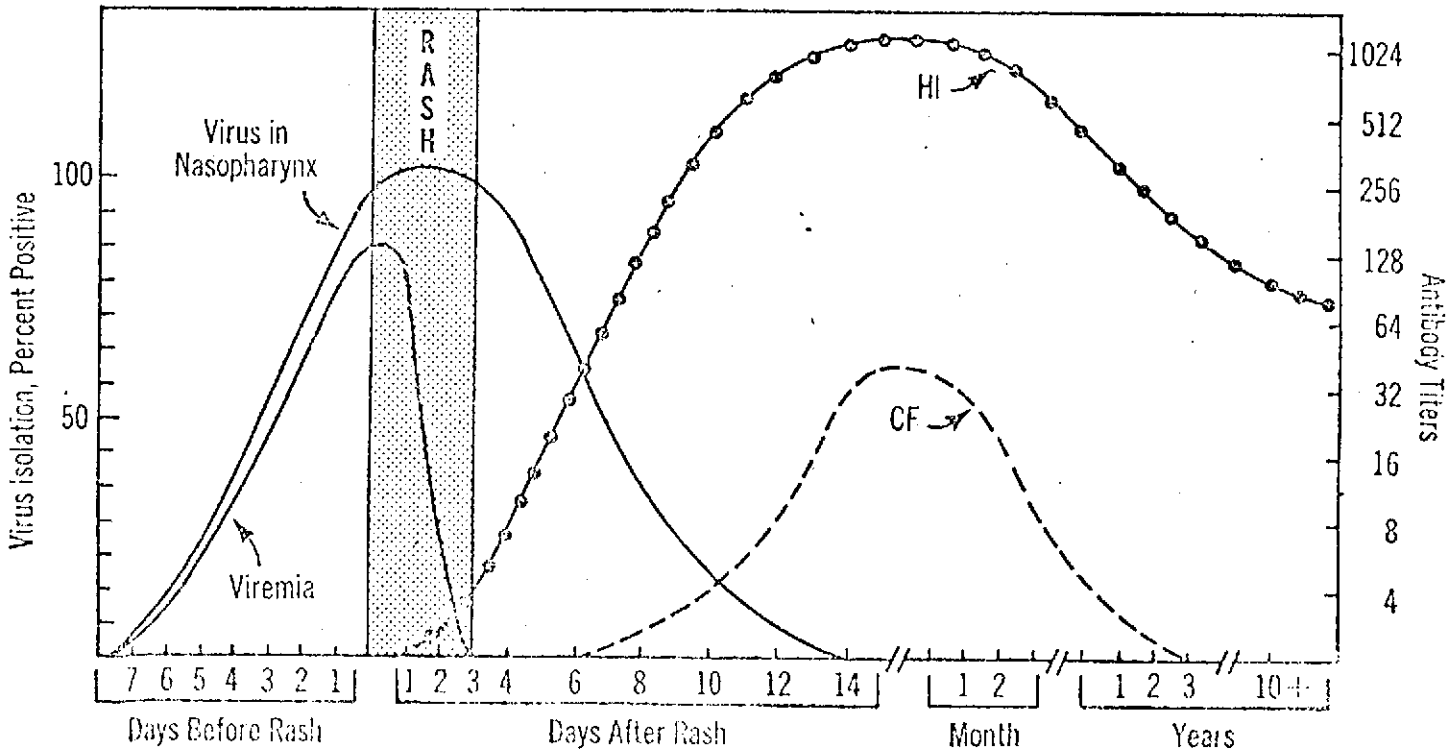
Determination of immunity status - HI suggested
Diagnosis of Detrology of viral exanthemata - CF or HI test on acute serum with a follow-up test on convalescent serum.

Comments:

Purified antigens are needed for all these assays. The present detection systems are sufficient to diagnose the disease 4-7 days following the appearance of a rash. The infective stage has passed by this time. Refer to Figure 1 below:

FIGURE 1

The appearance and disappearance of Rubella virus, HI and CF antibody.
(Abstracted from a teaching slide from the Center For Disease Control.)



2. Australia, SH or Hepatitus - Associated Antigen

Methods (arranged in order of decreasing sensitivity):

Radioimmunoassay
Hemagglutination inhibition
Complement fixation (CF)
Counterelectrophoresis (CEP)
Agar gel diffusion (AGD)

Clinical Use:

Used for detection of 30-40% of serum hepatitis cases.

Comments:

1. Lag between initial infection and the appearance of circulating antibody similar to rubella.
2. Antigen and antibody excess zones which will inhibit a positive reaction in all assays except the radioimmunoassay.
3. Lack of purified antigens.

3. Coccidiomycosis Antibody

Method:

Delayed hypersenstivity test
Slide Latex agglutination test
Immunodiffusion test

Clinical use:

Diagnosis of coccidiomycosis

Comments:

The delayed hypersensitivity test is specific, first to become positive and will remain positive life long.

Circulating antibody is only detectable 12 to 16 weeks following infection.

All serological tests for coccidiomycosis cross react with histoplasmesis and blastomycosis.

4. Treponema Pallidum Antibody Detection

Method:
Fluorescent Treponemal Antibody Absorption Test (FTA-ABS).

Clinical Use:
Diagnosis of syphilis > 90% effective.

Comments:
The FTA test uses specific T. pallidum antigen. There are some false positives related to cross reactivity between these antigens and similar,but undefined, determinates.

5. Toxoplasma Antibody Detection

Method:
Indirect hemagglutination (IHA)
Fluorescent antibody (FA)

Clinical Use:
Diagnose toxoplasmosis

Comments:
20-80% of the population has a positive titer (16-256). Rising titers are indications of active infection. New borns usually have a titer equivalent to the mother because of passive transfer.

6. Mycoplasma CF Test

Comment:
Antigens are cell extracts and cells are difficult to culture.

7. Endamoeba Histolytica

Method:
Direct exam of feces
Indirect Hemagglutination Test (IHA)
Complement Fixation Test (CF)

Comment:
Serum assays are good, but this microorganism is so distinctive and so easily identified that serum assays are probably unnecessary.

STEROID HORMONES

A. ANDROGENIC HORMONES

1. 17-Ketosteroids (17-KS)

Methods:

Colorimetric determination of all 17-Ketosteroids whether androgenic or not (Zimmermann test) (Refr.: Dreker, J. J. et al., J. Clin. Endocr. and Metab., 12:55, 1952)

Clinical Use:

a) Increased excretion occurs in:
Interstitial cell tumor of testes, very high
Simple hirsutism, occasionally
Cushing's syndrome due to adrenal hyperplasia
Adrenal hyperplasia-female pseudohermaphroditism or adrenogenital syndrome.
Adrenal cancer, virilism (not Cushing's syndrome), very high
Adrenal tumor, virilism, not malignant (?)
Arrhenoblastoma and lutein cell tumor of the ovary, when androgenic
Treatment with ACTH; Severe stress; Treatment with testosterone

b) Decreased excretion occurs in:
Thyrotoxicosis, Female hypogonadism, diabetes mellitus, hypertension, debilitating disease of mild to moderate severity - slight decrease.
Eunuchoidism or castration of male, gout, moderate to severe debility from any chronic illness - moderate decrease.
Addison's disease, panhypopituitarism, myxedema, nephrosis - severe decrease.

Comments:

If total 17-KS are normal there is little practical value to run either the DHA (dehydroepiandrosterone) determination by the Allen "blue" test or β:α

determination. The 17-KS can be grouped into the alpha fraction (principally androsterone and etiocholanolone) and the beta fraction (principally dehydroepiandrosterone.) The interpretation of a total 17-KS level in terms of androgenic activity must be made with consideration of the age, sex and clinical state of the patient. In most adult cases of adrenal carcinoma, the ratio of $\beta:\alpha$ ranges from 0.28-4.0. Most cases in children show a significant elevation of the ratio. A ratio of 0.4 or above indicates strongly carcinoma. Caution: there is a significant daily variation in 17-KS excretion.

Normal values:

Children:
Excretion rates are the same for both sexes through childhood. The following table indicates the range of values found:

Up to 1 yr.	= less than 1 mg. per day
1 - 4 yrs.	= less than 2 mgs. per day
5 - 8 yrs.	= less than 3 mgs. per day
13-16 yrs.	= 2.5-10 mgs. per day

Adult males:
9-22 mgs. per day. After about age 60 the rate of excretion progressively declines.

Adult females:
6-15 mgs. per day. After about age 60 the rate of excretion progressively declines.

The normal ratio of beta to alpha 17-ketosteroids is usually less than 0.2, i.e., there are at least five times as much alpha ketosteroids as beta ketosteroids by weight.

determination. The 17-KS can be grouped into the alpha fraction (principally androsterone and etiocholanolone) and the beta fraction (principally dehydroepiandrosterone.) The interpretation of a total 17-KS level in terms of androgenic activity must be made with consideration of the age, sex and clinical state of the patient. In most adult cases of adrenal carcinoma, the ratio of β:α ranges from 0.28-4.0. Most cases in children show a significant elevation of the ratio. A ratio of 0.4 or above indicates strongly carcinoma. Caution: there is a significant daily variation in 17-KS excretion.

Normal values:

Children:
Excretion rates are the same for both sexes through childhood. The following table indicates the range of values found:

Up to 1 yr.	= less than 1 mg. per day
1 - 4 yrs.	= less than 2 mgs. per day
5 - 8 yrs.	= less than 3 mgs. per day
13-16 yrs.	= 2.5-10 mgs. per day

Adult males:
9-22 mgs. per day. After about age 60 the rate of excretion progressively declines.

Adult females:
6-15 mgs. per day. After about age 60 the rate of excretion progressively declines.

The normal ratio of beta to alpha 17-ketosteroids is usually less than 0.2, i.e., there are at least five times as much alpha ketosteroids as beta ketosteroids by weight.

2. Testosterone

Methods:

Measurements of testosterone in plasma or serum determined by following techniques: bioassay, enzymatic-fluorescence, double isotope derivatization, partition chromatography, gas chromatography, competitive protein-binding radio assay, radioimmunoassay.

Clinical Use:

a) Adult Males:

Orchidectomy - concentration of testosterone drops down to 1/4 - 1/20 of the original level of the patient after being orchidectomized for neoplastic disease of the prostate or breast.

Estrogen Therapy - Patients with prostatic carcinoma treated with estrogen show a marked decrease in circulating testosterone.

Klinefelter's Syndrome - level of testosterone below lower limit of adult male.

Testosterone Therapy - patients with adult Leydig-cell failure or eunuchoidism.treated with long-acting testosterone esters show normal level for 2-3 weeks.

Primary and secondary hypopituitarism and hypogonadism - testosterone level below 200 nanograms/100 ml.

Hepatic cirrhosis - testosterone level between 110-550 nanograms/100 ml, but majority of cases are below 220 nanograms/100 ml.

b) Adult Females:

Polycystic Ovary (Stein-Leventhal Syndrome) - testosterone level between 100-300 nanograms/100 ml. ACTH or glucocorticoid treatment drops level of testosterone.

Idiopathic Hirsutism - testosterone level between 30-200 nanograms/100 ml. Synthetic glucocorticoid or estrogen-progesterone combinations reduce level to normal.

Virilizing Tumors - Arrhenoblastomas, dermoids, malignant teratomas and other tumors may secrete testosterone.

c) Prepubertal children:
Delayed puberty in young adults (15-17 years old): testosterone level below 100 nanograms/100 ml. Treatment possible (7-12 days) with human chorionic gonadotropism which increased the concentration 6-to 20-fold.

Pituitary infantilism in young adults: testosterone level below 100 nanograms/100 ml. Treatment showed no elevation of testosterone.

Comments:

Normal testosterone levels in men range from 300-1200 nanograms/100 ml. Studies show very little correlation of age and plasma testosterone.

Normal testosterone levels in women extend from 30-95 nanograms/100 ml. Levels are greater during the ovulatory and luteal phases of the menstrual cycle. During pregnancy concentration increases significantly (no relation to the sex of the fetus).

Concentration of plasma testosterone in children (4-10 years old) ranges for girls between 1-34 ng/100 ml and for boys 20-80 ng/100 ml.

Plasma testosterone level reflects a result of alterations of both the production rate and the metabolic clearance rate.

B. ESTROGENIC HORMONES

1. Total Estrogens Determination

Methods:

Fluorometric analysis - because of small quantities of the estrogens and interfering substances in the urine a purification utilizing gel filtration is necessary to obtain a sensitive and accurate measurement on a spectrophotofluorimeter.

Clinical Use:

a) Decreased Estrogen Values:

Agenesis of the ovaries
Primary ovarian malfunction
Dysfunction of the pituitary or other metabolic disturbances
Hypoestrogenism (absence of ovulation and corpus luteum function)
Inadequate sexual maturation or regression of previously occurring sexual maturation
Non-occurrence or cessation of menstruation
Absolute sterility
Hypofunction of the pituitary and adrenal glands may lead to low estrogen levels.

b) Increased Estrogen Values:

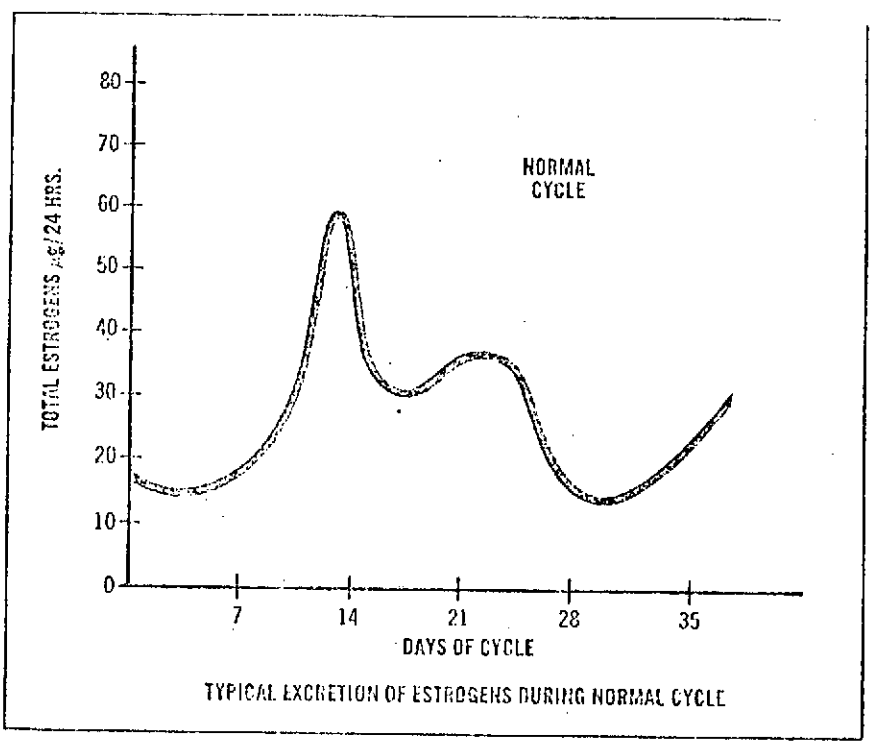
Ovarian tumors (cystic tumors comprise about two-thirds of all ovarian tumors, solid tumors are mostly granulosa- and theca-cell types).
A tumor or hypoplasia of the adrenal cortex may increase level. Cases in male may give rise to feminization with gynecomastia, impotence, azoospermia and testicular atrophy.

Comments:

The hyperestrogenism of a granulosa-cell or theca-cell tumor of the ovary during childhood should be differentiated from hyperovarianism.
Total urinary estrogen for non-pregnant or post-menopausal women and adult ment are:

Non-pregnant women-preovulatory phase: 5-25 micrograms/24 hr.
Non-pregnant woman-ovulatory phase: 24-100 micrograms/24 hr.
Non-pregnant women-luteal phase: 12-80 micrograms/24 hr.
Post-menopausal women: Less than 10 micrograms/24 hr.
Adult males: 4-25 micrograms/24 hr.

During pregnancy the estrogen level can rise as high as 45 milligrams per 24 hours.



TYPICAL EXCRETION OF ESTROGENS DURING NORMAL CYCLE

2. Placental Estriol

Methods:

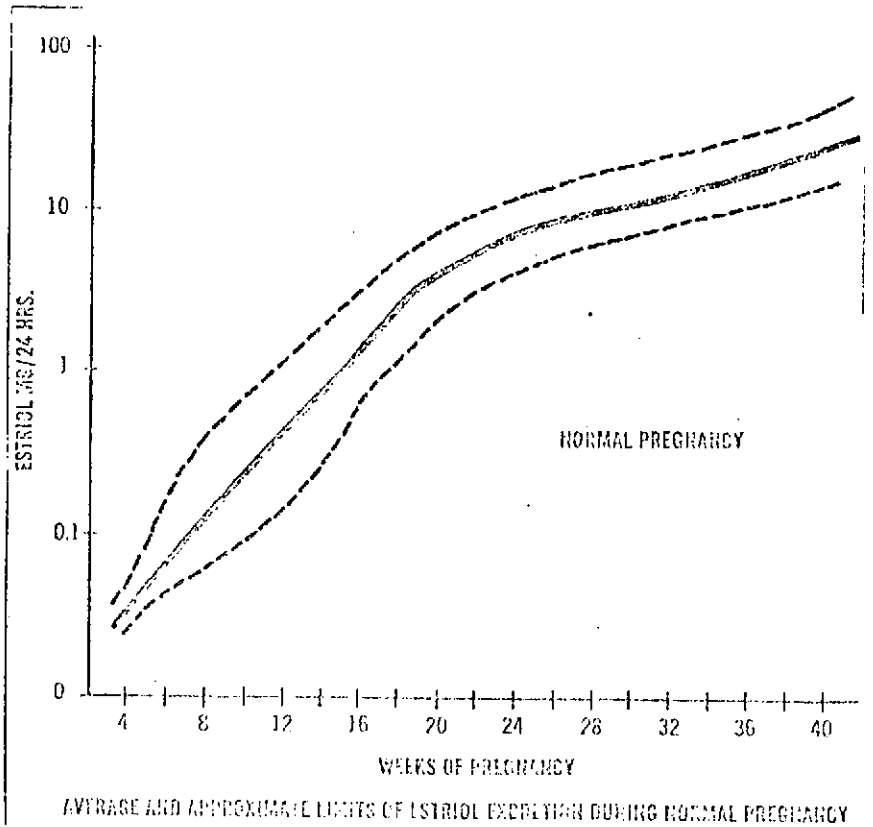
Chemical determination - high estriol content of pregnancy urine eliminates some of the complex purification procedures required in the Total Estrogen method.

Clinical Use:

Maternal urinary estriol excretion is a reliable index for assessment of the fetal placental complex. Decrease of estriol excretion during second and third trimesters may indicate placental dysfunction or other abnormalities of pregnancy.

Comments:

Serial determinations are essential since daily estriol values vary considerably. If estriol excretion curve declines constantly of more than 70% of previous values, placental insufficiency is probable.



AVERAGE AND APPROXIMATE LIMITS OF ESTRIOL EXCRETION DURING NORMAL PREGNANCY

Estriol excretion for the 2nd and 3rd trimester of pregnancy.

WEEKS OF PREGNANCY	RANGE OF ESTRIOL VALUES
16	Up to 3 mg/24 hrs.
20	1-9
24	4-12
28	5-17
32	6-22
36	8-32
40	9-37

C. PROGESTATIONAL HORMONES

1. Plasma Progesterone

Methods:

Specific binding of the hormone by corticosteroid-binding globulin (test is based on selective extraction of progesterone from plasma).

Clinical Use:

a) Females:

Infertility problems due to either Anovulatory Menstrual Cycles, Polycystic Ovary (Stein-Leventhal) Syndrome or Hypoplastic Secretory Endometrium (inadequate luteal phase) show low level of progesterone.

Adrenal Hyperplasia - uncomplicated virilizing adrenal hyperplasia (21-hydroxylase deficiency) elevates progesterone level.

Pregnancy - first trimester progesterone levels are equal or slightly higher as in the luteal phase of the normal menstrual cycle, thereafter, gradual increase occurs.

Threatened or Recurrent Abortion, Intrauterine Death - levels of plasma progesterone falls but in some cases of intrauterine death level remains normal for a period of time.

Poor Fetal Growth - no increase in progesterone values over a period of time may indicate poor fetal growth.

b) Males:
Virilizing Adrenal Hyperplasia - elevated progesterone levels, after ACTH stimulation level increases even more and may remain elevated if conversion to cortisol is impaired.

Comments:
Plasma progesterone levels are a more sensitive measure of corpus luteum formation than urinary pregnanediol.

Normal range of plasma progesterone in females:
Follicular phase - under 150 ng/100 ml.
Luteal phase - at least 300 ng/100 ml.
Peak levels at about mid-luteal phase may exceed 2,000 ng/100 ml.
Pregnancy values during first trimester range from 1500 - 5000 ng/100 ml and continues to rise and reaches values between 8,000 - 20,000 ng/ml in the third trimester.
Normal range of plasma progesterone in males: under 100 ng/100 ml.

2. Pregnanediol

Methods:
Quantitative assay of pregnanediol in urine using the chromatographic technic (Klopper, Midice, Brown, J. Endocr. 12 :209, 1955).

Clinical Use:
Threatened Abortion - lowered levels of pregnanediol, and if followed by high levels an abortion is very likely to happen.

Corpus Luteum Cysts - elevated levels of pregnanediol.

Remains of placental tissue in the uterus following parturition - elevated levels of pregnanediol.

Some cases of Adrenal-Cortical Tumors - show high levels.

Comments:
Degeneration of the corpus luteum and the onset of menstruation is evidenced by a precipitous decrease in urinary pregnanediol.
Proliferative phase: 0.5 - 1.5 mg/24 hrs.
Luteal phase: 2 - 7 mg/24 hrs.
Post menopausal levels range from 0.2 - 1.0 mg/24 hrs.

In pregnant females the pregnanediol excretion rises steady and at about the 32nd week it levels off. After 24 hrs. following parturition there is a drop to non-pregnancy levels by the 5th to the 10th day post-partum.

WEEKS OF PREGNANCY	RANGE OF PREGNANEDIOL IN URINE (MG./24 HRS.)
16	5—21
20	6—26
24	12—32
28	19—51
32	22—66
36	13—77
40	23—63

D. ADRENAL CORTICAL HORMONES - I: GLUCOCORTICOIDS

1. Urinary 17-OH-Corticosteroids

Methods:

a) 17-OH-corticosteroids may be determined as:
17-Ketogenic steroids (17-KGS)
Porter-Silber chromogens (e.g., Glenn-Nelson method)

b) 17-Ketogenic steroids include the 17-OH-corticosteroids with the dihydroxyacetone side-chain AND the pregnanetriol types of compounds.

c) Porter-Silber chromogens (Glenn-Nelson method) determine only the dihydroxyacetone side-chain compounds, e.g., THE, THF, and THS.

Clinical Use:

These hormones regulate gluconeogenesis (production of sugar to protein) which results in:
negative nitrogen balance
loss of potassium from tissues
decreased peripheral utilization of carbohydrate
insulin resistance (producing a diabetes)
increased uric acid excretion
increased circulating neutrophiles, eosinopenia, lymphopenia.

Overproduction or therapeutic administration of these hormones may result in the physical changes of Cushing's syndrome (thinning of skin, muscular wasting and weakness, osteoporosis and ecchymoses.

Comments:

The 17-KGS procedure is recommended for screening purposes from the standpoint of cost and the fact that it includes more 17-OH-corticosteroids.

NORMAL RANGE:

Urine:

BY 17-KETOGENIC STEROID METHOD:

AGE GROUP	MGS./24 HRS. MALE	FEMALE
Under 1 year	Less than 1	Less than 1
Up to 10 years	Less than 5	Less than 5
Adults	5 - 23	3 - 15
Over 70 years	3 - 12	3 - 12

BY GLENN-NELSON METHOD:

Adults	3 - 10	2 - 6

2. Plasma Cortisol (Plasma 17-OH-Corticosteroids)

Method:

Fluorescence technic - caution: plasma must be separated from the cells immediately after obtaining the heparinized blood; the fluorescence characteristics of the plasma cortisol are stable for at least 7 days at R.T. (30^{o} C).

Clinical Use:

17-OH-CORTICOSTEROID LEVEL	CLINICAL CONDITION
Low or low normal	Addison's disease
	Anterior pituitary hypofunction
Slight increase	Pregnancy (first trimester)
	Severe hypertension
	Virilism
Moderate increase	Stress: Infectious disease, surgery, burns, etc.
	Pregnancy (third trimester)
Marked increase	Cushing's syndrome, most cases
	Extreme stress: Pancreatitis, eclampsia

Comment:

Normal range of adults: 5-20 ng/100 ml plasma

The plasma cortisol determination may show spuriously elevated values if contraceptive drugs taken (increase in cortisol-binding protein from the use of estrogenic compounds).

3. Urinary "Free" (Unconjugated) Cortisol:

Methods:

Fluorimetric analysis - caution: spironolactone, an aldosterone antagonist, is a known interfering substance; estrogens and oral contraceptives may lead to elevated levels of urinary "free" cortisol.

Clinical Use:

Cushing's syndrome

Comment:

The procedure is primarily for uncovering elevations, low values do not necessarily indicate adrenal hypofunction. If high levels are found in patients taking contraceptive pills or other estrogenic material medication should be withheld and another estimation performed at least one month later.

Normal ranges:
Female: 78-365 μg/24 hours
Male: 108-409 μg/24 hours

D. ADRENAL CORTICAL HORMONES - II: MINERALOCORTICOIDS

1. Aldosterone

Methods:

Radioimmunoassay procedure for urinary aldosterone - method involves purification by extraction, followed by acid hydrolysis and re-extraction, and chromatography to remove naturally occurring steroids in potentially interfering levels. Radioimmunoassay involves the specific binding of aldosterone in competition with ^{3}H-aldosterone to an anti-aldosterone antiserum produced in sheep.

Clinical Use:

Secondary Aldosteronism -(aldosterone output is elevated due to a greater activity in the renin-angiotensin system or external stimuli).

a. Salt depletion, affecting the ECF.
b. Potassium loading, possibly through a transmembrane phenomenon.
c. ACTH in large doses, causing a transient rise.
d. Cardiac failure, effecting sodium retention and expansion of ECF. "Right-sided" heart failure apparently results in higher aldosterone levels.
e. Cirrhosis of liver with ascites formation.
f. Nephrotic syndrome.
g. Idiopathic cyclic edema, abnormal capillary permeability.
h. Pregnancy, increasing to term, followed by rapid decrease after delivery.
i. Bartter's syndrome, renal juxtaglomerular hyperplasia.
j. Post surgical syndrome.
k. Hypovolemia, hemorrhage, transudation and posture.

Primary Aldosteronism - high aldosterone output caused by an adrenocortical tumor in the face of low plasma renin activity. Hypertension, intermittent muscular pains, cramps, weakness, tetany, "paralysis" and polyuria.

Comment:

Normal range of urinary aldosterone at "Bio-Science" :2-26, µg per 24 hours (Note: assure adequate sodium intake).

The determination of plasma aldosterone is valuable in diagnosis and localization in primary aldosteronism. Plasma aldosterone is unstable at R.T., it is stable if kept frozen. Normal ranges are not precisely defined yet.

D. ADRENAL CORTICAL HORMONES - III: PREGNANETRIOL

Method:

Cox procedure - measuring the acetaldehyde formed upon oxidation of pregnanetriol with periodic acid.

Clinical Use:

Adrenogenital syndrome (e.g., congenital adrenal hyperplasia) - excessive excretion of pregnanetriol.

Comment:

Cases of adrenogenital syndrome often show a moderately elevated 17-Ketosteroid and a considerably increased 17-Ketogenic steroids (major fraction constituted by prenanetriol) level. Pregnanetriol is measured when urine is analyzed for 17-OH-corticosteroids by the 17-Ketogenic steroid procedure. By performing the 17-Ketogenic steroid test along with a pregnanetriol assay, information becomes available both as to the adrenal activity and metabolism.

Normal range found in urine of normal adults is 0.2 - 4 mgs/day. Children usually show less than 0.5 mgs/day. Pregnanetriol excretion is increased as a result of ACTH stimulation.

PROTEIN HORMONES

1. Chorionic Gonadotropin (CG)

Methods:

a) Bioassay - an aliquot of the urine is purified and concentrated by means of kaolin adsorption and elution at proper pH's. The extract is injected at various concentrations into immature (21 day old) female rats. After 24 hrs. the rats are sacrificed and the ovaries are examined for hyperemia as a possitive response.

b) Immunoassay - assays for CG have been performed by:
complement-fixation
precipitin tests
hemagglutination-inhibition tests with either sensitized erythrocytes or latex particles

Clinical Use:

Testicular tumors (usually mixed epithelioma type) - large amounts of CG (1,000 - 50,000 units) found in urine.
Chorionepithelioma - 100,000 units or more excreted CG.
Hydatidiform Mole - 100,000 units or more excreted CG.
Pregnancy test - hormone appears soon after the first missed menstruation in human pregnancy, reaches a peak between the 50th and 80th day of gestation then decreases until partically disappearing a few days after parturition.

Comment:

CG levels determined by immunological tests are somewhat higher than levels determined by bioassay. Normal range in male and non-pregnant female: none detected. In pregnant female CG levels in the immunoassay method reach 1,000 iu/liter between 35 to 40 days after the last normal menstrual period. Then level increases rapidly, peaking at about the 50th to 80th day. Decrease occurs and the level of 2,000 - 10,000 are maintained until parturition after which the hormone disappears within a few days.

2. Pituitary Gonadotropins

Methods:

Several methods have been employed for the bioassay of the pituitary gonadotropins, using as end points uterine enlargements, ovarian growth, vaginal patency, vaginal cornification, and seminal vesicle weights. The increase in uterine weight of the immature rat or mouse is the most widely used criterion and measures the combined FSH (Follicle Stimulating Hormone) and ICSH (Interstitial Cell Stimulating Hormone) effect on total gonadotropins.

Clinical Use:

Increased levels in:
Menopause, including premature menopause, Ovarian agenesis
Klinefelter's syndrome; Adult seminiferous tubule failure
Male climacteric

Decreased levels in:
Children before puberty; Hypogonadotrophic eunuchoidism
Anorexia nervosa; Estrogen administration
Neoplasms of the adrenal, ovary or testis which secrete estrogens or androgens

Comment:

NORMAL RANGE:

Urine by Bioassay:

Adults: Approximately 6-50 mouse uterine units (MUU) per 24 hours.
Children: (before puberty): Less than 6 MUU per 24 hours.
Menopausal: Greater than 50 MUU per 24 hours.

Serum or Plasma by RIA:

Male: 4-25 milli-IU/ml.

Female: Premenopausal—4-30 milli-IU/ml.
Postmenopausal—40-250 milli-IU/ml.
Midcycle peak—2x the baseline.

(Diurnal variations from high in the morning to low in the evening have been observed)

3. Luteinizing Hormone (LH)

Methods:

Radioimmunoassay procedure

(by Schalch, D.S., et al., J. Clin. Invest. 47:665, 1968) - the method utilizes serum as the specimen but is also capable of measuring LH in unconcentrated urine. Caution: Interfering substance is variably present in urine, so that a concentration and purification procedure would be necessary.

Clinical Use:

Amenorrhea due to ovarian failure - basal plasma LH levels are elevated (but not in case of amenorrhea secondary to pituitary failure) Caution: The mid-cycle peak is completely obliterated in normal women using oral contraceptives.

An ovulatory fertility problem - presence or absence of a mid-cycle peak can be established by analysis of a series of daily serum specimens. Caution: Difficulties in deciding when and how many specimens to collect. Schalch et al shows the mid-cycle to occur around the 11th - 17th day.

Postmenopausal state - testosterone and estrogen administered depresses LH levels.

Comment:

Normal Ranges:
Range in m I.U./ml. Serum

Men	Less than 11
Women, pre-menopausal	Less than 25
Women, mid-cycle peak	Greater than 3 times baseline value
Women, post-menopausal	Greater than 25

4. Insulin

Methods:

Radioimmunoassay determination - radioisotope-labeled insulin is added to sample with unlabeled insulin and the total insulin is reacted with a potent anti-insulin serum to form an insulin/anti-insulin complex. This complex is isolated by precipitation and the radioactivity determined of the unknown specimen.

Clinical Use:

Diagnosis of insulinoma - increase in plasma insulin level is greater after tolbutamide administration than after glucose.

Maturity-onset diabetes - the serum insulin level is higher than normal after ingestion of 100 grams of glucose between the 1 and 2 hour period.

Reactive hypoglycemia - elevated plasma insulin level along with normal blood glucose levels.

Acromegaly - elevated serum insulin level.

Comment:

NORMAL RANGE:

TIME (min.)	INSULIN (μU/ml.)
0	4 — 24
30	25 — 231
60	18 — 276
120	16 — 166
180	4 — 38

*Based on a statistical reanalysis of the data of Morgan and Holland.(5)

(5) Morgan, C.R., and Holland, W.M. III, Diabetes, 1966.

5. Growth Hormone

Method:

Radioimmunoassay technic - the hormone from the unknown specimen is made to compete with a fixed amount of isotope-labeled hormone (added to the unknown serum) for binding sites on

antibodies contained in a highly specific antiserum. Quantitated in a radiation counter, counts are fewer or greater in number depending upon the amount of growth hormone in unknown specimen.

Clinical Use:

Less than normal growth of humans or Dwarfism - hyposecretion of growth hormone by the pituitary gland.

Pituitary Giantism - hypersecretion of growth hormone.

Acromegaly - hypersecretion of growth hormone, characterized by gradual deformation of the bones particularly of the face, hands and feet.

Comment:

10% of drawfism in childhood may be caused by hyposecretion of growth hormone. It is important to distinguish these as early as possible since therapy with human growth hormone is effective. Since low levels are not significant, response to a challenge test is required.

A single, individual result is not significant in hypopituitarism, more information is usually obtained by the challenge tests.

Normal Range: The literature to date gives the following information for the fasting state.

BASELINE:	Adult Male:	0-8 nanograms/ml.
	Adult Female:	0-30 nanograms/ml.*
	Children:	0-10 nanograms/ml.

*(Lowest levels are found during basal conditions. Values in the upper end of this range may occur with special conditions such as Turner's syndrome, malnutrition, anorexia nervosa, obesity, or when high free fatty acid levels are present in the fasting state.)

FOLLOWING CHALLENGE:	(The GH response to challenge is usually less in children than in adults)
INSULIN:	30 min. to 2 hrs. after satisfactory insulin challenge: Baseline value increases 3-50 fold.
ARGININE:	30 min. to 1 hr. after appropriate arginine monohydrochloride* infusion: Male: Baseline value increases up to 3 fold. Female: Baseline value increases up to 10 fold. In general a rise in growth hormone concentration of 5 to 10 nanograms is considered a positive response to insulin and arginine stimulation tests.[13]
GLUCOSE:	30 min.-2 hrs. after 100g. glucose ingestion: Male or Female: Baseline value decreases to 0-3 nanograms/ml.

*Available from Cutter Laboratories as R-Genc®

6. Renin

Methods:

Bioassay - measures the amount of angiotensin II formed in the patient's plasma "in vitro" during a fixed time - temperature period.

Radioimmunoassay - the angiotensin I formed is incubated with specific antibody and ^{125}I-angiotensin I. The amount of ^{125}I-angiotensin I bound to antibody decreases with an increase in plasma angiotensin I as a result of competition for antibody sites.

Clinical Use: (See Page 20)

Clinical Use:

Recent reports on the renin-angiotensin system in various conditions in man*

Condition	PRA	Remarks
Physiologic		
Na depletion	+	—
Thiazide, short-term	+	—
long-term	0	—
long-term	+	Added sodium restriction
Cold pressor stimulation	+	—
Upright posture	+	—
Pharmacologic		
Catecholamines	+	—
Reserpine	—	—
Clonidine HCl (Catapres)	—	—
Hydralazine	+	—
Furosemide	+	—
Oral contraceptives	0, +	Also increases renin substrate
Sodium nitroprusside	+	—
Pregnancy		
Normal	+	—
Toxemic	+	Less than normal increase seen
Renal disease		
Glomerulonephritis	0	Canine experimental
Glomerulonephritis	0	Human nephritis
Nephrosis	+	—
Bineplectomy		—
Transplant	0	Normal response to stimuli
Obstructive uropathy with hypertension	+	—
Hypertension		
Renovascular	±	—
	+	Renal vein difference significant
Essential	—, 0	Response to stimuli sluggish in 25% of cases, especially in Negro
Malignant	+	—
Coarctation	0	—
Hypotension		
Postural	—	No rise with posture
Endocrine diseases		
Primary aldosteronism	—	—
Licorice hypertension	—	—
Bartter's syndrome	+	—
"Pseudoaldosteronism"	—	—
Pheochromocytoma	+	—
Congenital adrenal hyperplasia	+	Aldosterone secretion decreased
	—	DOC formed by lack of 11-hydroxylase
Miscellaneous diseases		
Cirrhosis with edema	+	—

PRA: + = increased; — = decreased; 0 = no change.
DOC = desoxycorticosterone.
*Drawn in most part from the medical literature, 1968 to 1969.

Comment:

NORMAL RANGES:
Bioassay:

PURPOSE AND CLINICAL CONDITION	Values in nanograms/100 ml. plasma	
	RECUMBENT (before arising, 7-8 A.M.)	UPRIGHT (following 4 hrs. of quiet, upright activity, about 12 noon)
To screen hypertensive patients:	(pt. off medication and on normal diet and salt as recommended below for three days prior to sampling)	
Normal	30-330*	73-490*
"Idiopathic" hypertension	Values usually fall within above range	Values usually fall within above range
Renovascular hypertension	335-8701‡	Usually elevated†
Frank primary aldosteronism	Very low (approaches zero)	Very low (approaches zero)
Malignant hypertension	450-4000†	Markedly elevated
To support tentative diagnosis of primary aldosteronism:	(pt. on low salt diet; no more than 10 meq./day for three days prior to sampling)	
Normal Response	25%-1000%** increase over baseline values obtained under screening conditions above	20%-225%** increase over baseline values obtained under screening conditions above
Frank primary aldosteronism	Very low (approaches zero)	Very low (approaches zero)
Possible primary aldosteronism	Low values	Low values

*95% confidence limits calculated by log transformation from the data of Gunnells, et al[9]

†Range (not statistical limits) found by Gunnells et al[9] on patients evaluated. For renovascular hypertension, 11 patients; for malignant hypertension, 13 patients.

**Range (not statistical limits) found by Gunnells for 16 patients.

‡Brown, et al[10] report that 75% of pts. with renal artery stenosis exhibit elevated renin levels, with severity correlating with degree of renin elevation.

Radioimmunoassay:
Renin activity is expressed as ng of angiotensin I released per ml of plasma per hour. For the upright position and normal salt intake in adults, the following range was established at Bio-Science Laboratories:

Normal Range = 0.4 - 4.5 ng/ml/hr.

7. Gastrin

Methods:

Radioimmunoassay - the serum gastrin is made to compete with a fixed amount of isotope - labeled synthetic gastrin for binding sites in an antiserum containing antibodies of high specificity.

Clinical Use:

Zollinger-Ellison (Z-E) syndrome - elevated serum gastrin levels, cases have been reported between 600-300,000 pg per ml.

Peptic ulcer disease - serum gastrin level of 400 pg/ml is not exceeded normally.

Pernicious anemia - elevated serum gastrin levels, disorder is characterized by the inability to secrete gastric HCl which can be quickly repaired by the intragastric infusion of 0.1N HCl.

Comment:

Normal range: Non-detectable to 300 pg gastrin/ml serum. Levels are considered elevated when clearly over 500 pg/ml. There is no statistically significant difference between the mean fasting serum gastrin level in patients with ulcer disease other than the Z-E syndrome and a population of patients without recognized ga-trointestinal diseases matched for age and sex.

ADRENAL MEDULLARY HORMONES

1. Catecholamines

Methods:

Determination of both the activation on fluorescence spectra with a recording spectrofluorometer of the urinary catecholamines.

Clinical Use:

Pheochromocytoma - elevated levels of urinary catecholamines.

Progressive muscular dystrophy - increased output of catecholamines.

Myasthemia gravis - increased output of catecholamines.

Comment:

The determination of urinary catecholamines corrolates well with the clinical state but there are situations which may lead to elevated levels not related to pheocromocytoma such as vigorous exercise prior to urine collection.
Medications which will lead to fluorescent urinary products are:

antihypertensive drugs of the alphamethyl dopa configuration
tetracycline antibiotics
large doses of the B vitamin complex
adrenaline and adrenaline-like drugs used in asthmatic seizures
carbon tetrachloride
erythromycin
hydralazine, quinine, quinindine, methenamine and formaldehyde.

Patients should be off such medications at least for one week.

2. Vanillylmandelic Acid (VMA)

Methods:

VMA is extracted from urine, oxidized to vanillin with periodate, vanillin is then purified by solvent partition and quantitated by its absorbance in the near ultraviolet (360 mμ).

Clinical Use:

a) confirmation of elevated catecholamine excretion
b) unexplained hypertension with normal catecholamine levels.
c) Neuroblastoma - produces high levels of VMA

Comment:

Medications, i.e. anilevidine, aspirin and methocarbamal and foods, i.e. coffee, fruits (bananas) and substances containing vanilla should be excluded before collecting sample.
Normal Range: 0.7-6.8 mg/24 hrs.

3. Metanephrines

Methods:

Urine is hydrolyzed, the metanephrines are separated by Amberlite CG-50 cation exchange resin and oxidized by periodate to vanillin which is assayed spectrophotometrically at 360 mμ

Clinical Use:

Parameter for determining the abnormal catecholamine production.

Comment:

Normal range: 0.3-0.9 mg/24 hrs.

4. Homovanillic Acid (HVA)

Methods:

Colorimetric determination - HVA reacts with nitrosonaphthol in nitrous acid and produces the color.

Clinical Use:

Neuroblastomas
Ganglioneuromas

Comment:

Certain cases of neurological tumors show that the urinary abnormality consists almost entirely of excessive excretion of dopamine and its metabolite, HVA.
Normal range: up to 15 mg/24 hrs.

ENZYMES

1. Glutamic-Oxalacetic-Transaminase (SGO-T)

Method:

Clinical Use:

Myocardial infarction - following infarction serum SGO-T level begins to rise in about 4-6 hours. A peak level ranging from 2-20 times the upper limit of normal occurs within 24-48 hours after the onset.
Pulmonary embolism - increased levels.
Congestive failure with infarcts and other organs - increased levels.
Pancreatitis - increased levels
Skeletal muscle damage (including post-surgery) - increased levels.
Myositis - increased levels.
Liver diseases - SGP-T is actually more sensitive than SGO-T to hepatocellular damage.
Neurological disorders - increased levels, they are not consistently altered in cases of brain tumors.

Comment:

Since SGO-T is found in all tissues, it is not unexpected that a false positive would occur in certain disease states.
In a suspected case of myocardial infarction a sample should be taken as soon as possible to use assa baseline, and to take serial determinations for several days.
Normal values: in serum 12-40 units
in spinal fluid 5-73 units.

2. Serum Glutamic-Pyruvic Transaminase (SGP-T)

Methods:

Clinical Use:

Liver disease - in acute hepatitis or carbon tetrachloride poisoning values over 500 units are usually found.
Acute myocardial infarction - increased levels except in extensive necrosis or hepatic damage resulting from congestive heart failure.

Comment:

In hepatitis the elevations of SGP-T and SGO-T begins several weeks before other tests indicate liver damage.
In cirrhosis and metastatic carcinoma levels are quite variable.
Normal values: 11-66 units in male, 5-53 units in female.

3. Lactic Dehydrogenase (LDH)

Methods:

Clinical Use:

a) Serum LDH elevations in: cirrhosis, hepatitis, metastatic involvement of the liver, pulmonary embolism, progressive muscular dystrophy, megaloblastic anemia, infectious mononucleosis, infarcation, transplantation and homograft rejection.

b) LDH increases in cerebrospinal fluid in: degerative diseases of the central nervous system, convulsive disorders, head injuries, subarachnoid hemorrhage, meningitis, lymphoma, leukemia, carcinoma.

c) LDH activity of pleural and peritoneal effusions increased in: containing or in contact with malignant cells.

d) Elevated levels in urine LDH in: cancer of kidneys or bladder, in glomerulonephritis, malignant hypertension, lupus nephritis, acute tubular necrosis, renal transplantations and homograft rejection, sometimes in pyelonephritis.

Comment:

Normal values of LDH:
a) in serum - 63-to 155 units in male; 62-131 units in female.
b) in spinal fluid - 13 to 80 units.
c) in urine - up to 8300 units/8 hrs.

4. LDH Isoenzymes

Methods:

Clinical Use:

Myocardial infarction - isoenzymes one and two increases in serum.

Liver disease - isoenzyme five increases

Comment:

Normal values:

ISOENZYME	% OF TOTAL ACTIVITY	TYPE
1	15-30	Cardiac
2	22-50	Cardiac
3	15-30	---
4	0-15	---
5	0-15	Hepatic

5. Aldolase

Methods:

Clinical Use:

Acute viral hepatitis - markedly elevated levels.
Progressive muscular dystrophy - high elevated levels.
Myocardial infarction - elevated levels.
Acute pancreatitis - elevated levels.
Diseases involving tissue damage - elevated levels.

Comment:

Normal range: 13-31 units in male, 11-22 units in female.

6. Creatine Phosphokinase

Methods:

Clinical Use:

Myocardial infarction
Progressive muscular dystrophy
Polymyositis
Hypothyroidism
Muscular trauma
Myonecrosis
Myoglobinuria
Severe physical exertion

Comment:

Normal range: up to 4.3 units in male, up to 2.5 units in female. No elevated levels in pulmonary infarction or in parenchymal liver damage.

7. α-Hydroxybutyric Dehydrogenase (HBD)

Methods:

Clinical Use:

Myocardial infarction

Large increase in HBC - activity:
Progressive muscular dystrophy
Nephrotic syndrome
Malignant melanoma
Lymphoma
Leukemia
Megaloblastic anemia

Chronic and acute liver diseases

Comment:

Normal range: 140-350 units. It has been reported that elevation of HBD is more specific and prolonged than that of SGO-T or LDH in cases of myocardial infarction.

8. Isocitric Dehydrogenase (ICD)

Methods:

Clinical Use:

Liver diseases - ICD levels are sensitive reflections of acute hepatic necrosis.

Comment:

Normal range: 50-260 units.

9. 5'-Nucleotidase

Methods:

Clinical Use:

Liver diseases

Comment:

Normal range: 0-1.6 units. In liver diseases the activity of 5'-Nucleotidase parallels the serum alkaline phosphatase but does not increase in rickets or Paget's disease.

10. Alkaline Phosphatase Isoenzymes

Methods:

Determination of the percent thermostable fraction of serum AP - an aliquot of serum is heated for 10' at 56°, the AP concentration of unheated and heat treated serum is then determined.

Clinical Use:

The percent thermostable fraction has no significance for serum AP values in the normal range, but for elevated serum AP levels.

a) Values of greater than 35%. Hepatic disease or disease with liver being the predominant tissue involved.

b) Values of 25% to 35%. A combination of hepatic and skeletal disease in various proportions.

c) Values of less than 25%. Skeletal disease with increased osteoblastic activity.

Paget's disease of bone - liver isoenzyme responsible for elevated AP.

Malabsorption - bone isoenzyme elevated.

Cirrhotics - intestinal isoenzyme mostly responsible for elevated AP.

Tumors - the so-called Regan isoenzyme has been found in about 3% of patients.with variety tumors.

Comment:

Normal range: total serum AP activity is 4-17 (King-Armstrong Units).
Revealing the thermolability of bone enzyme and the relative thermostability of liver AP, it was concluded that hypatobiliary enzyme could be distinguished from skeletal enzyme by heating for 10 min. at 56°.

11. Gamma Glutamyl Transpeptidase (GGT)

Methods:

Note: GGT enzyme test is an exquisitely sensitive measure of pathological processes occurring in the liver.

Clinical Use:

Note: GGT enzyme test is an exquisitely sensitive measure of pathological processes occurring in the liver.

Chronic and subacute hepatitis - increased GGT - level.
Cirrhosis of the liver - increased GGT - level.
Intra- or extrahepatic obstruction disease - elevated GGT - level.

Malignancies in liver, bile ducts, head of the pancrease - markedly increased GGT-level.
Detection of liver damage due to alcoholism - GGT determination is more sensitive than the transaminases.

Comment:

Normal range in serum is for males under 28 mU/ml, for females under 18 mU/ml, for adolescents under 45 mU/ml.

12. Red Cell Enzymes

Methods:

G-6-PD Quantitative test

Red Cell Enzyme Screening Tests (G-6-PD Screening test - visual detection of a fluorescent spot is consistent with the presence of the enzyme in the hemolysate, while a dark UV-adsorbing spot indicates absence of the enzyme).

Clinical Use:

Glucose-6-Phosphate Dehydrogenase (G-6-PD) Deficiency - three major types of G-6-PD-deficiency:

a) type A, found in black subjects
b) Mediterranean type, found in Caucasians and Orientals
c) the rare congenital, non-spherocytic anemia

Pyruvate Kinase deficiency - hemolytic anemia, no additional distinguishing or pathognomonic clinical features.

Triosephosphate Isomerase (TPI) deficiency - red cell TPI deficiency shows a severe hemolytic anemia together with a progressive neurologic disorder.

NADH Diaphorase deficiency - accumulation of methemoglobin which is characterized in life-long cyanosis.

Glutathione Reductase - congenital non-spherocytic hemolytic anemia.

APPENDIX 7

VIRUSES WHICH REQUIRE PURIFICATION

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/Test/Titer)		Bacterial Sterility	Mycoplasam	Refer.
V-001-511-553	Picornavirus Enterovirus Poliovirus	1	LSc 2ab	Other viruses (Virus/test/titer) Coxsackie A-9 (Griggs) Coxsackie B-3 (Nancy) ECHO 4 (DuToit) ECHO 11 (Gregory)	ECHO 11/SN/10 vs 26TCID$_{50}$	Neg	--	44, 47
V-002-511-560	Picornavirus Enterovirus Polio	2	P-712	Other viruses (Virus/test/titer) Polio Types 1, 3 Coxsackie A Types 7, 9 Coxsackie B Types 1-6 ECHO Types 1-32	Polio 1/SN/1:58 Polio 3/SN/1:20	Neg	--	44, 47
V-005-501-563	Picornavirus Enterovirus Coxsackie	A-2	Fleetwood	Other viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1, 2, 3 Simian-27 Types	SV-6/SN/1024 SV-19/SN/128	Neg	--	28, 145*
V-006-501-563	Picornavirus Enterovirus Coxsackie	A-3	Antiserum	Other viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1, 2, 3 Simian Types-27 types	Coxsackie A-8/SN≥16 SV-19/SN/256 Coxsackie A-17/CF/17 SV-29/SN/2048 Coxsackie A-19/CF/16 Coxsackie A-20/CF/24 Coxsackie A-24/CF/32 SV-32/SN/1:32 SV-37/SN/1:32	Neg	--	28, 145*
V-007-501-563	Picornavirus Enterovirus Coxsackie	A-4	Alabama 4-CDC	Other viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1, 2, 3 Simian-27 Types	Coxsackie A-5/CF/32 SV-32/SN/64 SV-37/SN/32 SV-19/SN/760	Neg	--	28, 145*

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	References
					Coxsackie A3/SN/1:32	Neg	--	28, 145*
V-008-501-563	Picornavirus Enterovirus Coxsackie	A-5	Swartz	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	Coxsackie A-12/SN(both M&TC)/≤1:80 Coxsackie A-12/CF/1:28 (recip cross) ECHO 18/SN/1:16 Coxsackie A-18/CF/1:30 (recip cross) Coxsackie A-14/CF/1:64 Coxsackie A-17/CF/1:32 (recip cross) Coxsackie A-20/CF/1:16 (recip cross) SV-27/SN/1:64 SV-37/SN/1:25 SV-19/SN/1:32			
V-009-501-563	Picornavirus Enterovirus Coxsackie	A-6	Gdula	Other Viruses(Virus/test/titer) Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	Coxsackie A-2/CF/1:128 Coxsackie A-4/CF/1:128 Coxsackie A-5/CF/1:128 Coxsackie A-12/CF/1:128 Coxsackie A-14/CF/1:128 Coxsackie A-16/CF/1:90	Neg	--	28, 145*
V-010-501-563	Picornavirus Enterovirus Coxsackie	A-7	AB-IV (USSR)	Other Viruses (Virus/test/titer) Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	Coxsackie A-5/SN inM/≥1:80 Coxsackie A-8/SN(both M&TC) ≥1:20 ECHO 23/SN/1:16 Coxsackie A-14/CF/1:45 Coxsackie A-16/CF/1:32 Coxsackie A-17/CF/1:20 Coxsackie A-20/CF/1:20	SV-32/SN/1:32 SV-37/SN/1:64 SV-6/SN/1:1600 SV-26/SN/1:512 SV-35/SN/1:5000 Neg	-- --	28, 145*
V-011-501-563	Picornavirus Enterovirus Coxsackie	A-8	Donovan	Other Viruses (Virus/test/titer) Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	Cox A-3/SN/1:20 (recip cross) Cox A-3/CF/1:90 Cox A-5/SN/≥1:120 Cox A-5/CF/1:56 Cox A-10/SN/1:175 (recip cross) Cox A-10/CF/1:45 Cox A-12/SN/1:24 Cox A-12/CF/1:256	Cox A-14/CF/1:128 Cox A-20/CF/1:32 SV-30/SN/1:25 SV-32/SN/1:32 SV-37/SN/1:32 SV-6/SN/1:800 Neg	-- --	28, 145*

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	References
				Other viruses (Virus/test/titer)				
V-012-501-563	Picornavirus Enterovirus Coxsackie	A-9	P.B(Bozek)	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1-18 Simian - 27 Types	Coxsackie A-6/CF/1:24 Coxsackie A-10/CF/1:24 Coxsackie A-11/CF/1:32 Coxsackie A-23/CF/1:24 Coxsackie A-24/CF/1:24 SV-32/SN/1:32 SV-29/SN/1:40	Neg	--	28, 145*
V-013-501-563	Picornavirus Enterovirus Coxsackie	A-10	Kowalik	Other Viruses (Virus/test/titer) Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	CoxsackieA-8/SN/1:24(recip cross) Coxsackie A-24/SN/≥1:16 ECHO 21/SN/1:16 Coxsackie A-5/CF/1:24 (recip cross) Coxsackie A-7/CF/1:24 Coxsackie A-14/CF/1:32 SV-32/SN/1:64 SV-37/SN/1:25 SV-6/SN/1:800 SV-29/SN/1:128	Neg	--	28, 145*
V-014-501-563	Picornavirus Enterovirus Coxsackie	A-11	Belgium-1	Other Viruses (Virus/test/titer) Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	Cocsackie A-17/SN/1:16 ECHO 23/SN/1:16 Coxsackie A-2/CF/1:16 SV-32/SN/1:100 SV-37/SN/1:25 SV-6/SN/1:800 SV-19/SN/1:32 SV-40/SN/1:40	Neg	--	28, 145*
V-015-501-563	Picornavirus Enterovirus Coxsackie	A-12	Texas-12	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	Coxsackie A5/CF/1:128 (recip cross) Coxsackie A-14/CF/1:45 SV-32/SN/1:64 SV-37/SN/1:128 SV-4/SN/1:64	Neg	--	28, 145*
V-016-501-563	Picornavirus Enterovirus Coxsackie	A-13	Flores	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	Coxsackie A-5/CF/1:16 Coxsackie A-11/SN/1:16 Coxsackie A-18/SNinTC/1:100 (recip cross) Coxsackie A-18/SNinM/1:570 (recip cross) SV-32/SN/1:32 SV-19/SN/1:64 SV-4/SN/1:32	Neg	--	28, 145*

Catalog #	Virus Group	Type Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	References
V-017-501-563	Picornavirus Enterovirus Coxsackie	A-14 G-14	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	ECHO 23/SN/1:16 SV-27/SN/1:24 SV-32/SN/1:32 SV-37/SN/1:32 SV-29/SN/1:100	Neg	--	28, 145
V-018-501-563	Picornavirus Enterovirus Coxsackie	A-15 G-9	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	SV-27/SN/1:32 SV-32/SN/1:32 SV-36/SN/1:40 SV-37/SN/1:32 SV-19/SN/1:32 SV-4/SN/1:64	Neg	--	28,145 *
V-019-501-563	Picornavirus Enterovirus Coxsackie	A-16 G-10	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	Coxsackie A-4/CF/1:128 Coxsackie A-15/CF/1:32 Coxsackie A-23/CF/1:128 SV-32/SN/1:32 SV-37/SN/1:25 SV-19/SN/1:25 SV-29/sN/1:640 SV-4/SN/1:50	Neg	--	28, 145
V-020-501-563	Picornavirus Enterovirus Coxsackie	A-17 G-12	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	Coxsackie A-24/SNinTC/≥1:16 (recip cross) Coxsackie A-24/SNinM/1:28 ECHO 17/SN/≤1:20 ECHO 21/SN/1:16 Coxsackie A-5/CF/1:32 (recip cross) SV-17/SN/1:25 SV-37/SN/1:32	Neg	--	28, 145
V-021-501-563	Picornavirus Enterovirus Coxsackie	18 G-13	Simian-27 Types Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3	Coxsackie A-13/SN(TC)/≥1:256 (recip cross) Coxsackie A-13/SN(M)/1:2100 (recip cross) Coxsackie A-11/SN/1:17 Coxsackie A-14/SN/1:32 ECHO 5/SN/≥1:16 SV 32/SN/1:32 SV 36/SN/1:40 SV 37/SN/1:100 SV 29/SN/1:160 SV 4/SN/1:128	Neg	--	28, 145*

Catalog #	Virus Group	Type Strain	Other Viruses (Virus/test/titer)	Bacterial Sterility	Mycoplasma	References
V-023-501-563	Picornavirus Enterovirus Coxsackie	A-20 I.H.35	Other Viruses (Virus/test/titer) Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian-27 Types	Cox A-8/SNinTC≥1:32 Cox A-17/SNinSM/1:80 Cox A-20a/SNinSM/>1:2000 Cox A-20a/CF/1:28 (recip cross) Cox A-20b/SNinSM/>1:1260 Cox A-5/CF/1:16 (recip cross) Cox A-6/CF/1:64 SV-32/SN/1:25 SV-37/SN/1:40 SV-6/SN/1:250 SV-4/SN/1:64	Neg	--	28, 145*
V-023A-501-563	Picornavirus Enterovirus Coxsackie	A-20a Tulane 1623	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3	Coxsackie A-20/SN(TC)/1:40 (recip cross) Coxsackie A-20/SN(M)/1:130 (recip cross) Coxsackie B-20b/SN(TC)/1:125 (recip cross) Coxsackie B-20b/SN(M)/1:400(recip cross) SV-32/SN/1:25 SV-29/SN/1:320 SV-4/SN/1:128	Neg	--	28, 145*
V-023B-501-560	Picornavirus Enterovirus Coxsackie	A-20b Cecil	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1,2,3 Simian 27 Types	Coxsackie A-20/SNinTC/1:400 Coxsackie A-20/SNinM/≥1:1260 Coxsackie A-20/CF/1:80 Coxsackie A-20a/SNinM≥1:2000 Coxsackie A-20a/CF/1:64 (recip cross) SV-32/SN/1:40 SV-37/SN/1:128 SV-35/SN/1:50	Neg	--	28, 145*
V-024-501-563	Picornavirus Enterovirus Coxsackie	A-21 Kuykendall	Polio Types 1, 2, 3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1, 2, 3 Simian-27 Types	ECHO 23/SN/<1:16 Coxsackie A-5/CF/1:32 Coxsackie A-12/CF/1:32 Coxsackie A-14/CF/1:20 SV-15/SN/1:32 SV-37/SN/1:25 SV-37/SN/1:64 SV-19/SN/1:100 SV-29/SN/1:128	Neg	--	28, 145*
V-025-501-563	Picornavirus Enterovirus Coxsackie	A-22 Chulman	Other viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1, 2, 3 Simian-27 Types	Coxsackie A-20a/CF/1:24	Neg	--	28, 145*

Catalog #	Virus Group	Type	Strain	Other Viruses (Viruses	(Virus/test/titer)		Bacterial Sterility	Mycoplasma	Refer.
V-027-501-563	Picornavirus Enterovirus Coxsackie	A-24	Joseph	Polio Types 1, 2, 3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-32 Adeno Types 1-18 Reovirus Types 1, 2, 3 Simian-27 Types	Coxsackie A-17/SN in TC/ 1:24 (recip cross) Coxsackie A-17/SN in SM/≤1:16 (recip cross) ECHO 23/SN/1:32 Coxsackie A-4/CF/1:32 SV-27/SN/1:25 SV-37/SN/1:64		Neg	--	28, 145*
V-028-501-563	Picornavirus Enterovirus Coxsackie	B-1	Conn-5	Polio Types 1, 2, 3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-30 Adeno Types 1-18 Simian-27 Types	Coxsackie B-5/SN/1:160 SV-4/SN/1:32 SV-23/SN/1:20 SV-32/SN/1:25 Coxsackie B-6/CF/1:16		Neg	--	102, 117* 152*
V-029-501-563	Picornavirus Enterovirus Coxsackie	B-2	Ohio-1	Polio Types 1, 2, 3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-30 Adeno Types 1-18 Simian-27 Types	SV-4/SN/1:32 SV-23/SN/1:16 SV-27/SN/1:20 SV-31/SN/1:16 Coxsackie B-2/CF/1:32 Coxsackie B-6/CF/1:32	SV-19/SN/1:40 SV-26/SN/1:20 SV-29/SN/1:16 SV-32/SN/1:32 Neg	 Neg	 --	 102, 117* 152*
V-030-501-563	Picornavirus Enterovirus Coxsackie	B-3	Nancy	Polio Types 1, 2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-30 Adeno Types 1-18 Simian-27 Types	ECHO 7/SN/1:16 SV-19/SN/1:100 SV-27/SN/1:20 SV-32/SN/1:40 Coxsackie B-17/CF/1:16 Coxsackie B-6/CF/1:16	SV-4/SN/1:32 SV-24/SN/1:20 SV-31/SN/1:18 Neg	 Neg	 --	 102, 117* 152*
V-031-501-563	Picornavirus Enterovirus Coxsackie	B-4	JVB	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-30 Adeno Types 1-18 Simian-27 Types	SV-1/SN/1:16 SV-20/SN/1:16 SV-26/SN/1:20 Coxsackie B-1/CF/1:16 Coxsackie B-6/CF/1:16	SV-4/SN/1:32 SV-24/SN/1:20 SV-32/SN/1:25 Neg	 Neg	 --	 102, 117* 152*
V-032-501-563	Picornavirus Enterovirus Coxsackie	B-5	Faulkner	Polio Types 1, 2, 3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-30 Adeno Types 1-18 Simian-27 Types	SV-4/SN/1:40 SV-23/SN/1:20 SV-26/SN/1:20 SV-27/SN/1:20 SV-32/SN/1:16 Coxsackie B-1/CF/1:16 Coxsackie B-6/CF/1:16		Neg	--	102, 117* 152*

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	References
V-033-501-563	Picornavirus Enterovirus Coxsackie	B-6	Schmitt	Polio Types 1,2,3 Coxsackie A Types 1-24 Coxsackie B Types 1-6 ECHO Types 1-30 Adeno Types 1-18 Simian-27 Types	SV-30/SN/1:16 SV-31/SN/1:32 SV-32/SN/1:40 Coxsackie B01/CF/1:64	Neg	--	102, 118*, 152*
V-034-501-560	Picornavirus Enterovirus ECHO	1	Farouk	Polio Types 1,2,3 Coxsackie A Types 7,9 Coxsackie B Types 1-6 ECHO Types 2-32	ECHO 8/SN/1:300	Neg	--	
V-034-501-563	Picornavirus Enterovirus ECHO	1	Farouk	Polio Types 1,2,3 Coxsackie A Types 7, 9, 11, 13, 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 Types	ECHO 8/CF/1:128 (recip cross) ECHO 8/SN/1:1000 SV-20/SN/1:20 SV-25/SN/1:20 Sv-34/SN/1:20	Neg	--	99*
V-036-501-563	Picornavirus Enterovirus ECHO	3	Morrisey	Other Viruses (Virus/test/titer) Polio Types 1,2,3 Coxsackie A Types 7,9,11 13, 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 Types	ECHO 7/SN/≥1:100 SV-10/SN/1:32	Neg	--	99*
V-037-501-563	Picornavirus Enterovirus ECHO	4	Pesascek	Other Viruses (Virus/test/titer) Polio Types 1,2,3 Coxsackie A Types 7, 9, 11 13, 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 Types	Adeno 8/SN/≥1:320 SV-19/SN/1:80 SV-23/SN/1:16	Neg	--	99*

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	Reference
V-038-501-560	Picornavirus Enterovirus ECHO	5	Noyce	Other Viruses (Virus/test/titer) Polio Types 1,2,3 Coxsackie A Types 7, 9 Coxsackie B Types 1-6 ECHO Types 1-4, 6-32	ECHO 3/SN/1:200 ECHO 8/SN/1:56 ECHO 11/SN/1:16 ECHO 12/SN/1:250 ECHO 19/SN/1:23	Neg	--	
V-038-501-563	Picornavirus Enterovirus ECHO	5	Noyce	Other Viruses (Virus/test/titer) Polio Types 1,2,3 Coxsackie A Types 7,9,11, 13, 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 Types	SV-19/SN/1:80	Neg	--	99 *
V-039-501-563	Picornavirus Enterovirus ECHO	6	D'Amori	Other Viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7,9,11,13 15, 18 Coxsackie B Types 1-25 ECHO Types 1-25 Adeno Types 1-10 Simian-21 Types	ECHO 19/SN/≤1:30 Cox B3/SN1:40 SV-17/SN/1:20 SV-19/SN/1:20	Neg	--	99*
V-039B-501-563	Picornavirus Enterovirus ECHO	6	Burgess	Other Viruses (Virus/test/titer) Polio Types 1,2,3 Coxsackie A Types 7, 9, 11, 13 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 types	ECHO 14/SN/<1:32 SV-19/SN/1:32 SV-22/SN/1:20 SV-23/SN/1:16	Neg	--	71, 99*
V-041-501-563	Picornavirus Enterovirus ECHO	8	Bryson	Other Viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7, 9, 11, 13 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10	ECHO 1/SN/1:3000 ECHO 1/CF/1:32 SV-17/SN/1:24 SV-22/SN/1:20 SV-23/SN/1:80 SV-26/SN/1:20	Neg	--	99*

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	Refer.
V-042-511-563	Picornavirus Enterovirus ECHO	9	Visop	Other Viruses(Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 3, 7-18, 20a, 20b, 20c, 21, 23, 24 Coxsackie B Types 1-6 ECHO Types 1-28 Reovirus Types 1, 2, 3 Enterovirus Type 59+Candidates Caldwell & Pett	Coxsackie A-23/SN/1:4096	Neg	Neg	145*
V-044-501-563	Picornavirus Enterovirus ECHO	11	Gregory	Other Viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7, 9, 11, 12 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 Types	ECHO 17/SN/<1:128 ECHO 19/SN/<1:32 SV-12/SN/1:20 SV-15/SN/1:20 SV-17/SN/1:20 SV-18/SN/1:20 SV-22/SN/1:16 SV-26/SN/1:20	Neg	--	99*
V-045-501-563	Picornavirus Enterovirus ECHO	12	Travis	Other Viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 3, 7 - 18, 20a, 20b, 20c, 21, 23, 24 Coxsackie B Types 1-6 ECHO Types 1-28 Reovirus Types 1, 2, 3 Enterovirus Type 59 + Candidates Caldwell + Pett	ECHO 1/SN/1:256 ECHO 1/CF/1:128	Neg	--	99* 156
V-046-501-563	Picornavirus Enterovirus ECHO	13	DelCarmen	Other Viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7, 9, 11, 13 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian - 21 Types	Coxsackie A-7/SN/1:25 SV-19/SN/1:20 SV-22/SN/1:20 SV-23/SN/1:16	Neg	—	99*

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	Refer.
V-049-501-563	Picornavirus Enterovirus ECHO	16	Harrington	Other Viruses(Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7, 9, 11, 13 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 Types	ECHO 17/SN/1:40 Adeno 3/SN/1:16 SV-15/SN/1:20 SV-17/SN/1:16 SV-18/SN/1:16	Neg	--	99*
V-050-501-563	Picornavirus Enterovirus ECHO	17	CHHE 29	Other Viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7, 9, 11, 13 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 types	Adeno7/SN<1:16 SV-17/SN/1:20 SV-19/SN/1:20	Neg	--	99*
V-052-501-563	Picornavirus Enterovirus ECHO	19	Burke	Other Viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7, 9, 11, 13 15,18 ECHO Types 1-25 Adeno Types 1-10 Simian-21 types	ECHO 7/SN/<1:16 ECHO 11/SN≤1:40 SV-17/SN/1:16	Neg	--	99*
V-053-501-563	Picornavirus Enterovirus ECHO	20	JV-1	Other Viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7, 9, 11, 13, 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 types	SV-12/SN/1:23 SV-18/SN/1:20 SV-20/SN/1:20 SV-23/SN/1:20 ECHO 21/CF/1:64	SV-17/SN/1:32 SV-19/SN/1:20 SV-22/SN/1:20 SV-27/SN/1:16 Neg	--	99*

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	Ref.
V-055-501-563	Picornavirus Enterovirus ECHO	22	Harris	Other viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7, 9, 11, 13 15,18 Coxsackie B Types 1 - 6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 Types	Coxsackie B-4/SN/≤1:64 SV-17/SN/1:24 SV-27/SN/1:20	Neg	--	99*
V-056-501-563	Picornavirus Enterovirus ECHO	23	Williamson	Other viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7, 9, 11, 13 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian - 21 Types	ECHO 11/SN/≤1:16 ECHO 22/SN/ 1:256 Coxsackie A-9/SN/≥1:16 Coxsackie B-4/SN≥1:16	Neg	--	99*
V-057-501-563	Picornavirus Enterovirus ECHO	24	DeCamp	Other Viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7, 9, 11, 13 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 Types	ECHO 19/SN/1:63 Coxsackie B-4/SN/≥1:50 SV-17/SN/1:32 SV-27/SN/1:20	Neg	--	99*
V-058-501-563	Picornavirus Enterovirus ECHO	25	JV-4	Other viruses (Virus/test/titer) Polio Types 1, 2, 3 Coxsackie A Types 7, 9, 11, 13, 15, 18 Coxsackie B Types 1-6 ECHO Types 1-25 Adeno Types 1-10 Simian-21 Types	Coxsackie B-4/SN/≥1:16 SV-1/SN1:25	--	--	99*
V-113-501-053	Picornavirus Rhinovirus	1B	B-632	Other viruses(Virus/test/titer) 1A, 1A(JH), 1B, 1B(k779), 2, 3, 4, 5, 6, 13, 14, 15, 16, 17, 23 (100319), 34, 35, 36, 37, 39, 40, 41, 42, 42(248A0, 44, 49.	Rhinovirus type 1B(K778)/SN/1:192	Neg	--	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)	Bacterial Sterility	Mycoplasma	Ref.
V-107-501-053	Picornavirus Rhinovirus	2	HGP	Other viruses (Virus/Test/Titer) 1A, 1A(JH), 1B, 1B(K779), 2, 3, 4, 5, 6, 13, 14, 15, 16, 17, 23 (100319), 26(127-1), 29(179E), 30, 31, 32, 33, 34, 35, 56, 37, 39, 40, 41, 42, 42(248A), 44, 49.	Rhinovirus type 2/SN/1:64 Neg	--	--
V-119-501-053	Picornavirus Rhinovirus	3	Antiserun	Other viruses (Virus/test/titer) 1A, 1A(JH), 1B, 1B(K779), 2, 3, 4, 5, 6, 13, 14, 15, 16, 17, 23 (100319), 26 (127-1), 29(179E), 30, 31, 32, 33, 34, 35, 56, 37 39, 40, 41, 42, 42(248A), 44, 49	Rhinovirus type 17/SN/1:48 Neg	--	--
V-120-501-053	Picornavirus Rhinovirus	6	Thompson	Other viruses (Virus/test/titer) 1A, 1A(JH), 1B, 1B(K779), 2, 3, 4, 5, 6, 13, 14, 15, 16, 17, 23 (100319), 26(127-1), 29(179E), 30, 31, 32, 33, 34, 35, 36, 37, 39, 40, 41, 42, 42(248A), 44, 49.	Rhinovirus type 35/SN/1:48 Neg	--	--
V-102-501-053	Picornavirus Rhinovirus	13	353	Other viruses (Virus/test/titer) 1A, 1A(JH), 1B, 1B(K779), 2, 3, 4, 5, 6, 13, 14, 15, 16, 17, 23 (100319), 26(127-1), 29(179E), 30, 31, 32, 33, 34, 35, 36, 37, 39, 40, 41, 42, 42(248A), 44, 49.	Rhinovirus type 41/SN/1:48 Neg	--	--
V-140-511-053	Picornavirus Rhinovirus	23	100319	Other viruses (Virus/test/titer) 1A, 1A(JH), 1B, 1B(K779), 2, 3, 4, 5, 6, 13, 14, 15, 16, 17, 23 (1000319), 26(127-1), 29(179E), 30, 31, 32, 33, 34, 35, 36, 37, 39, 40, 41, 42, 42(248A), 44, 49.	Rhinovirus type 49/SN/1:256 30/SN/1:48 Neg	--	--
V-108-501-053	Picornavirus Rhinovirus	32	363	Other viruses (Virus/test/titer) 1A, 1A(JH), 1B, 1B(779), 2, 3 4, 5, 6, 13, 14, 15, 16, 17, 23 (100319), 26(127-1), 29(179E), 30, 31, 32, 33, 34, 35, 36, 37, 39, 40, 41, 42, 42(248A), 44, 49.	Rhinovirus type 1A/SN/1:384 Neg	--	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	Ref.
V-167-511-053	Picornavirus Rhinovirus	42	248A	Other viruses (virus/test/titer) 1A, 1A(JH), 1B, 1B(K779), 2, 3, 4, 5, 6, 13, 14, 15, 16 17, 23(100319), 26(127-1), 29,(179E), 30, 31, 32, 33, 34, 35, 36, 37, 39, 40, 41, 42, 43(248A), 44, 49.	Rhino.-5/SN/52 13/SN/>16 42/SN/512 17/SN/48 4/SN/48 26(127-1)/SN/32	Neg	--	97, 119, 127, 134, 140, 147, 149, 155
V-116-501-053	Picornavirus Rhinovirus	49	8213	Other viruses (Virus/test/titer)	Rhinovirus type 2/SN/1:192	Neg	--	--
V-148-501-057	Picornavirus Rhinovirus	--	611-CV35	Other viruses (Virus/test/titer) Coryzavirus Types 34 thru 54	CV41/SN/1:40	--	--	154A
V-207A-501-565	Adenovirus (Human)	7a	S-1058	Other viruses (Virus/test/titer) Adeno Types 1 - 30	Adeno 11/HI/1:20-40 Adeno 14/HI/1:20-320	Neg	Neg	93, 138*
V-208-501-565	Adenovirus (Human)	8	Trim	Other viruses (Virus/test/titer) Adeno Type 1-30	Adeno 9/HI/1:320-1:640 Adeno 10/HI/1:40-1:80	Neg	Neg	93 138*
V-209-501-565	Adenovirus (Human)	9	Hicks	Other viruses (Virus/test/titer) Adeno types 1-30	Adeno 8/HI/1:60-1:320	Neg	Neg	93 138*
V-210-501-565	Adenovirus (Human)	10	J.J.	Other viruses (Virus/test/titer) Adeno Types 1 - 30	Adeno 19/HI1:160-1:820	Neg	Neg	92 138*
V-211-501-565	Adenovirus (Human)	11	Slobitski	Other viruses (Virus/test/titer) Adeno Types 1-30	Adeno 7a/HI/1:40 Adeno 7a/SN/1:20-1:40 Adeno 14/HI/1:160-1:640 Adeno 14/SN/1:20-1:160 Adeno 21/SN/1:16-1:80	Neg	Neg	93 138*
V-212-501-565	Adenovirus (Human)	12	Huie	Other viruses (Virus/test/titer) Adeno Types 1-28	Adeno Type 18/SN/1:10-1:150	Neg	Neg	93 138*

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	Ref.
V-214-501-565	Adenovirus (Human)	14	DeWit	Other viruses (Virus/test/titer) Adeno Types 1-30	Adeno 7a/HI/1:10-1:160 Adeno 7A(SN)1:20-1:40 Adeno 11/HI/1:40 Adeno 11/SN/1:20-1:40	Neg	Neg	93 138*
V-215-501-565	Adenovirus (Human)	15	CH. 38	Other viruses (Virus/test/titer) Adenovirus type 1-30	Adeno 22/HI/1:20-1:80 Adeno 29/SN/1:160-1:640	Neg	Neg	93 138*
V-216-501-565	Adenovirus (Human)	16	CH79	Other viruses (Virus/test/titer) Adeno Types 1-30	Adeno 4/SN/1:120-1:1280	Neg	Neg	93 138*
V-219-501-565	Adenovirus (Human)	19	3911	Other viruses (Virus/test/titer) Adeno Types 1-30	Adeno 10/HI/indication of cross by some labs.	Neg	Neg	93 138*
V-223-501-565	Adenovirus (Human)	23	2732	Other viruses (Virus/test/titer) Adeno Types 1-30	Adeno 15/SN1:30-1:256 Adeno 29/SN/indication of cross by some labs	Neg	Neg	93 138*
V-224-502-565	Adenovirus (Human)	24	3153	Other viruses (Virus/test/titer) Adenovirus types 1-30	Adeno 8/HI/1:40 Adeno 19/HI/1:40 Adeno 21/SN/1:20-1:80	Neg	Neg	93 138*
V-225-501-565	Adenovirus (Human)	25	BP-1	Other viruses (Virus/test/titer) Adenovirus types 1-30	Adeno 15/SN/Indication of cross by some labs	Neg	Neg	93 138*
V-229-501-565	Adenovirus (Human)	29	BR-6	Other viruses (Virus/test/titer) Adeno Types 1-30	Adeno 15/SN/1:32-1:2560 Adeno 23/SN/1:16-1:160 Adeno 9 + Adeno/25/SN - indicated cross by some labs	Neg	Neg	93 138*
V-230-501-565	Adenovirus (Human)	30	BP-7	Other viruses (Virus/test/titer) Adeno Types 1-30	Adeno 13/SN/indicated cross by some labs	Neg	Neg	93 138*
V-231-501-565	Adenovirus (Human)	31	1315	Other viruses (Virus/test/titer) Adenovirus Types 1-30	Adeno T-12/SN/1:320 Adeno T-18/SN/1:20	Neg	Neg	41, 106, 124 148

Catalog #	Virus Group	Type Strain	Other Viruses (virus/test/titer)		Bacterial Sterility	Mycoplasma	Refer.
V-301-501-552	Myxovirus	Infl.A Swine/1976/31	Other viruses (Virus/test/titer) Infl. A-PR-8, FM-1, Jap/305, Jap/305 Lot 2, Jap/170 Infl. B - Lee, GL, Md, Taiwan Infl. C - Taylor Para 1-HA-2, Sendai Para 2-Greer, SV-5 Para 3-SF-4, Mumps, NDV, Measles	A-PR-8/HI/1:20 A-FM-1/HI/1:20 B-Taiwan/HI/1:10 ($K10_4$) C-Taylor/HI/1:20 (RDE) 1:20 ($K10_4$)	Neg	Neg	--
V-301-511-552	Myxovirus	Infl.A PR-8/34	Other viruses (Virus/test/titer) Infl. A - Swine, FM-1, Jap/305 Jap/305 lot 2, Jap/170 Infl. B - Lee, GL, Md, Taiwan Infl. C - Taylor Para 1 - HA-2, Sendai Para 2 - Greer, SV-5 Para 3 - SF-4, Mumps, NDV, Measles	B-Taiwan/HI/1:10 (RDE) 1:10 ($K10_4$) C-Taylor/HI/1:40 (RDE) 1:40 ($K10_4$)	Neg	Neg	--
V-301-521-552	Myxovirus	Infl. A-1 FM-1/47	Other viruses (Virus/test/titer) Infl. A - Swine, PR-8, Jap/305, Jap/305 lot 2, Jap/170 Infl. B - Lee, GL, Md, Taiwan Infl. C - Taylor Para 1 - HA-2, Sendai Para 2 - Greer, SV-5 Para 3 - SF-4, Mumps, NDV, Measles	B-Taiwan/HI/1:10 ($K10_4$) C-Taylor/HI/1:20 (RDE) 1:20 ($K10_4$)	Neg	Neg	--
V-301-531-552	Myxovirus	Infl. A-2 Japan/305/57	Other viruses (Virus/test/titer) Infl. A - Swine, PR-8, FM-1, Jap/170 Infl. B - Lee, GL, Md, Taiwan Para 1 - HA-2, Sendai Para 2 - Greer, SV-5 Para 3 - SF-4, Mumps, NDV, Measles	A-Jap/170/HI/1:800 B-Taiwan/HI/1:10 ($K10_4$) C-Taylor/HI/1:20 (RDE)	Neg	Neg	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	Refer.
V-301-541-552	Myxovirus	Infl. A-2	Japan/ 170/62	Other viruses (Virus/test/titer) Infl. A - Swine, PR-8, FM-1, Jap/305, Jap/305 lot Infl. B - Lee, GL, Md, Taiwan Infl. C - Taylor Para 1 - HA-2, Sendai Para 2 - Greer, SV-5 Para 3 - SF-4, Mumps, NDV, Measles	A-Jap/305/HI/1:160 A-Jap/305 lot 2/HI/1:160 B-Taiwan/HI/1:10 ($K10_4$) C-Taylor/HI/1:20 (RDE) 1:20 ($K10_4$)	Neg	Neg	--
V-301-551-552	Myxovirus	Infl. A-2	Taiwan/ 1/64	Other viruses (Virus/test/titer) Influ A: PRS/1-M-1/Swine/Equine-1 Equine-2/WS/Japan 170 Japan 305/Taiwan Influ B: Lee/Maryland/GreatLakes/ Taiwan/Singapore Influ C: Taylor Para 1 : HA-2 Para 2 : Greer/SV-5 Para 3 : S1--4 NDV	A-Japan-305/H1/1:80, SN/1:20 Japan-170/H1/1:40, SN/1:20	Neg	Neg	--
V-301-561-552	Myxovirus	Infl. A	Equine-1/Prague 56	Other viruses (Virus/test/titer) Influ A: PR8/FM-1/Swine/Equine-1 Equine-2/WS/Japan 170 Japan 305/Taiwan Influ B: Lee/Maryland/Great Lakes/ Taiwan/Singapore Influ C: Taylor Para 1 : HA-2 Para 2 : Greer/SV-5 Para 3 : SF-4	A-Japan-305/H1/1:30, SN/1:20 Japan-170/H1/1:40, SN/120	Neg	Neg	
V-301-571-552	Myxovirus	Infl. A	Equine-2/Miami/ 1/63	Other viruses (Virus/test/titer) Influ A: PR8/FM-1/Swine/Equine-1 Equine-2/WS/Japan 170 Japan 305/Taiwan Influ B: Lee/Maryland/Great Lakes/ Taiwan/Singapore Influ C: Taylor Para 1: HA-2 Para 2: Greer/SV-5 Para 3: SF-4 NDV	A-Japan-305/HI/1:80, SN/1:20 Japan-170/HI/1:40, SN/1:20	Neg	Neg	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)	Bacterial Sterility	Mycoplasma	Refer.
V-301-581-552	Myxovirus	Infl. A	WS/33	Other viruses (Virus/test/titer) Influ A: PR8/FM-1/Swine/Equine-1 Equine-2/WS/Japan 170 Japan 305/Taiwan Influ B: Lee/Maryland/Great Lakes/ Taiwan/Singapore Influ C: Taylor Para 1: HA-2 Para 2: Greer/SV-5 Para 3: SF-4 NDV	Neg A-PR8/HI/1:80, SN/1:20(200)	--	--
V-301-591-552	Myxovirus	Infl. A-2	Aichi/2/ 68	Other viruses (Test/Virus/Titer)	SN/flu A-Swine, PR8, FM, B Lee, B Md., B Taiwan, B Sing, B Mass., P1, P2 (Greer & SV-5), P3, C Taylor, A equi/1:<10; A2 Japan 170, A Equi, NDV; A2 Japan 305, A2 Taiwan/ 1:20; HI/ flu A-Swine, PR8, FM, WS, A equi Prague; B Lee, B Md, B Taiwan, B Sing, B Mass, C Taylor/ <10; A2 Japan 305 & 170, A2 Taiwan/1:40; A equi 2 Maimi/1:10; NDV/1:20 Neg	Neg	--
V-301-591-558	Myxovirus	Infl. A-2	Aichi/ 2/68	Other viruses (Test/virus/titer)	SN/flu A-Swine, PRS, FM, Equi, flu B Md, TW, Sing, NDV, P1 (C-35), P2 (Greer & SV-5), P3 flu C/<10, flu B Lee/1:10; flu B Mass/ 1:20; flu A Jap 305, Jap 170/1:40; flu A equi 2/1:80; flu A Tw/1:160. CF/A (Soluble)/1:64; B(Soluble), C(GL), P1, P2, P3, Mumps, P2(SV-5), NDV, NAF/<8 HI/flu A-Swine, A-WS-33, A-PR-8-34, A1-FM-1-47, A-Equi 1 Prague, A-Equi 2 Miami, B Lee, B Md, B Taiwan, B Sing, B Mass, NDV, C Taylor/<10; A2 Japan-305, A2 Japan 170/1:10;A2 Taiwan 1:80 Neg	Neg	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	Ref
V-302-501-552	Myxovirus	Infl. B	Lee/40	Other viruses (Virus/Test/Titer) Infl. A - Swine, PR-8, FM-1, Jap/305, Jap/305 lot 2, Jap/170 Infl. B - GL, Md, Taiwan Infl. C - Taylor Para 1 - HA-2, Sendai Para 2 - Greer, SV-5 Para 3 - SF-4, Mumps, NDV, Measles	B-GL/HI/1:40 B-Md/HI/1:40 B-Taiwan/HI/1:80 (RDE) 1:10 ($K10_4$) C-Taylor/HI/1:40 (RDE)	Neg	Neg	--
V-302-511-552	Myxovirus	Infl. B	GL/1739 54	Other viruses (Virus/test/titer) Infl. A - Swine, PR-8, FM-1, Jap/305, Jap/305 lot 2, Jap/170 Infl. B - Lee, Md, Taiwan Infl. C - Taylor Para 1 - HA-2, Sendai Para 2 - Greer, SV-5 Para 3 - SF-4, Mumps, NDV, Measles	B-Lee/HI/1:40 B-Md/HI/1:300 B-Taiwan/HI/1:80 (RDE) 1:80 ($K10_4$) C-Taylor/HI/1:40 (RDE) 1:20 ($K10_4$)	Neg	Neg	--
V-302-521-552	Myxovirus	Infl. B	Maryland 1/59	Other viruses (Virus/test/titer) Infl. A - Swine, PR-8, FM-1, Jap/305, Jap/305 lot 2, Jap/170 Infl. B - Lee, GL, Taiwan Infl. C - Taylor Para 1 - HA-2, Sendai Para 2 - Greer, SV-5	B-Lee/HI/1:80 B-GL/HI/1:320 B-Taiwan/HI/1:320 (RDE) 1:60 ($K10_4$) C-Taylor/ HI/1:40 (RDE) 1:20 ($K10_4$)	Neg	Neg	--
V-302-531-552	Myxovirus	Infl. B	Taiwan 2/62	Other viruses (Virus/test/titer) Infl. A - Swine, PR-8, FM-1, Jap/305, Jap/305 lot 2, Jap/170 Infl. B - Lee, GL, Md Infl. C - Taylor Para 1 - HA-2, Sendai Para 2 - Greer, SV-5 Para 3 - SF-4, Mumps, NDV, Measles	B-Lee/HI/1:40 B-GL/HI/1:80 B-Md/HI/1:80 C-Taylor/HI/1:40 (RDE) 1:20 ($K10_4$)	Neg	Neg	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	Ref.
V-302-541-552	Myxovirus	Infl. B	Singapore 3/64	Other Viruses (virus/test/titer) Influ A: PR8/FM-1/Swine/Equine-1 Equine-2/WS/Japan 170 Japan 305/Taiwan Influ B: Lee/Maryland/Great Lakes/ Taiwan/Singapore Influ C: Taylor Para 1: HA-2 Para 2: Greer/SV-5 Para 3: SH-4 NDV	B-Great Lakes/HI/1:10 Maryland/HI/1:40, SN/1:40 Taiwan/HI/1:10	Neg	Neg	--
V-303-501-552	Myxovirus	Infl. C	Taylor 1233/47	Other viruses (Virus/test/titer) Infl. A - Swine, PR-8, FM-1, Jap/305, Jap/305 lot 2, Jap.170 Infl. B - Lee, GL, Md, Taiwan Para 1 - HA-2, Sendai Para 2 - Greer, SV-5 Para 3 - SF-4, Mumps, NDV, Measles	A-Jap/170/HI/1:40	Neg	Neg	--
V-321-501-558	Myxovirus Parainfluenza	1	HA-2 C-39	Other viruses (Virus/test/titer) Influenza A, B, & C Para 1-Sendai Para 2-Greer, SV-5 Para 3-SF-4, HA-1 Para 4-M-25 Mumps, RSV Measles, CD, NDV, ICH	Para 1-Sendai/HI/1:20, CP/1:80, SN/1:20	Neg	Neg	--
V-321-511-558	Myxovirus Paramyxovirus Parainfluenza	1	Sendai	Other Viruses (Virus/test/titer) Para 1 - HA_2 Para 3 - SF-4	Para 1-HA_2HI/1:10 Para 1-HA_2/CF/1:80 Para 1-HA_2/SN/1:10	Para 3-SF-4/HI/1:20 Para 3-SF-4/CP/1:10 Mumps/CF/1:20		
				Mumps	Mumps/SN/1:20	Neg	Neg	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)	Other Viruses (Test/Virus/Titer)	Bacterial Sterility	Mycoplasma	Ref.
V-322-503-558	Myxovirus Parainfluenza	2	Greer, CA	Other Viruses (Test/Virus/Titer)	Neut,CF, HI/P1(HA-2), P1(Sendai), P2(SV-5, P3(HA1, P3(SF), Mumps, Measles, NDV, Flu A, Flu B/<1:10 Neut, CF/P4A(M-25), P4B(19503), RS(Long) RS(18537)/<1:10 CF. HI/Flu C/≤1:10 HI/Adeno Grp., Eaton Agent/≥ 1:10	Neg	Neg	83, 116A
V-322-502-558	Myxovirus Parainfluenza	2	Greer, CA	Other Viruses (Test/Virus/Titer)	Neut CF,HI/P1(HA-2),P1(Sendai), P3(HA-1) P3(SF), Flu A, Flu B, Mumps, Measles, NDV/≤1:10 Neut, CF/P2(SV-5), P4A(M-25), P4B(19503), RS(Long), RS(19537)/1:10 CF,HI/Flu, C/≤1:10 HI/P2(SV-5)/≤1:40 CF/Adeno Grp, Eaton Agent/≤1:10	Neg	Neg	83, 116A
V-322-512-558	Myxovirus Parainfluenza	2-SV_5	21005-2WR	Other Viruses (Test/Virus/Titer)	Neut, CF, HI/P1(Sendai), P1(HA-2), P2(Greer), P3(HA-1), P3(SF), NDV, Mumps, Flu A, Flu B/≤1:10 Neut, CF/P4A(M-25), P4B(19503), RS(Long) RS(19537)/≤1:10 CF/Adeno Group, Eaton Agent/≤1:10 CF, HI/Flu C/≤1:10	Neg	Neg	144A 156

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)	Bacterial Sterility	Mycoplasma	Refer.
V-323-502-558	Myxovirus Parainfluenza	3	HA-1	Other Viruses (Test/Virus/Titer)	Neut,CF, HI/P1(Sendai), P1(HA-2), P2 (Greer), P2(SV-5), NDV, Measles, Flu A, Flu B/≤1:10 Neut, CF/P4A(M-25), P4B(19503), Mumps, RS(Long), RS(19537/≤1:10 Neut/P3(SF)/1:20 CF/P3(SF)/1:80 Flu C, Adeno Grp. Eaton Agent/ ≤1:10 HI/P3(SF)/1:320 Mumps/1:40 Flu C/≤1:10	Neg	Neg	--
V-325-502-558	Myxovirus Paramyxovirus Mumps	--	Enders	Other Viruses (Virus/Test/Titer) Para 2 - (SV-5) Para 2 - (Greer) Para 3 - (HA-1)	Para 2-SV-5/HI/1:10-1:20	Neg	Neg	--
V-326-501-558	Myxovirus Paramyxovirus	Newcastle Disease Virus	Roakin	Other viruses (Virus/Test/Titer) Para 1 - Sendai Para 2 - SV-5	Para 2-SV-5/HI/1:80 Para 2-SV-5/CP/1:10 Para 1 - Sendai/CH/1:20	Neg	Neg	--
V-327-501-558	Myxovirus	Respiratory syncytial	Long	Other Viruses (Test/Virus/Titer)	P1(Sendai), P2(HA-2), P2(SV-5), P2(Greer) P3(HA-1), P3(SF), P4A(M-25), P4B(19503), Mumps Measles, NDV, Flu A, Flu B/<1:10 Neut/RS(18537), RS(1075)/1:10 CF/Flu C, Adeno Grp. Eaton Agent/≤1:10, RS(18537)/1:40, RS(1075)/1:80	--	Neg	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)	Bacterial Sterility	Mycoplasma	Refer.
V-329-501-555	Myxovirus, Canine Distemper Virus	--	Lenderle Avirulent	Other viruses (Virus/test/titer) Measles Infectious Canine Hepatitis	Neg	Neg	--
V-346-501-558	Herpesvirus	Herpes Simplex	Mayo 1814	Other viruses (Virus/test/titer) Herpes simplex (HF) Herpes simplex (McIntyre) B Virus (E-2490) B Virus (Sabin) Pseudorabies (Aujesky)	Herpes simplex (HF)/SN/1:128 Herpes simplex (McIntyre)/SN/1:128 B Virus (E-2490)/SN/1:4 potentiated B Virus (Sabin)/SN/1:4 potentiated Neg	Neg	--
V-347-501-558	Herpesvirus	B	Lilly E-2490	Other viruses (Virus/test/titer) Herpes simples (HF) Herpes simplex (McIntyre) B Virus (E-2490) B Virus (Sabin) Pseudorabies (Aujeszky)	Neg. B virus (Sabin)/SN/1:8 nonoptentiated Herpes simples (McIntyre)/SN/1:128 B Virus (E-2490)/SN/1:4 potentiated B Virus (Sabin)/SN/1:4 potentiated Neg.: B Virus (Sabin)/SN/ 1:16 potentiated	Neg	--
V-348-501-558	Herpesvirus	Pseudorabies Aujeszky		Other viruses (Virus/Test/Titer) Pseudorabies (Kaplan) Herpes simplex (Mayo 1814) Herpes simplex (MF) Herpes simplex (McIntyre) B Virus (E-2490) B Virus (Sabin)	Pseudorabies (Kaplan)/SN/1:64 B Virus (E-2490)/SN/1:4 potentiated B Virus (Sabin)/SN/1:4 potentiated Neg	Neg	--

Catalog #	Virus Group Type	Strain	Other Viruses (Virus/test/titer)	Bacterial Sterility	Mycoplasma	Refer.
V-501-701-562	Bwamba Bwamba	Smithburn (M459)	Other Arboviruses (Test/Virus/Titer) CF/Bunyamwera - unassigned 1 Neg; Group Capim 1 Neg; Group Patois 1 Neg; Group Guama 1 Neg; Small Groups 6-8, 9a, 9d, 10, 10a, 11a, 13, 14a, 16, 16a, 16b Neg; Group VSV 4 Neg; Ungrouped 1, 2, 8, 10-13, 15, 16, 19, 20, 28, 29, 31, 32, 35-51 Neg; HI/Group A 1, 2, 4, 5 Neg; Group B 3, 7, 11, 15, 17, 23, 26, 27, 31, 33, 35, 37 Neg; Group C 6, 8, Neg; 7 (+1/10); Group Patois 1, 2, Neg; Group Bunyamwera 1-3, 6-10, 13 Neg; 12 (+1/10); Group Phlebotomus 1, 2, 4-6, 8, 11 Neg; Group Simbu 2-4 Neg; 8 (+1/10); Minor Groups 2, 2b, 3, 4, 4a, 10a, 15, 15a, 15b Neg; Ungrouped 32, 36, 43 Neg; Group California 2, 6, 9, 10 Neg; Group Capim 4 Neg;	Neg	Neg	--
V-502-701-562	California California Encephalitis BFS 283		Other arboviruses (Test/Virus/Titer) CF Bunyamwera-Unassigned 1 Neg; Group Capim 1 Neg Group Patois 1 Neg; Group Guama 1 Neg; Small Groups 6-8, 9a, 9d, 10, 10a, 11a, 13 14a, 16, 16a, 16b Neg; Group VSV 4 Neg; Ungrouped 1, 2, 8, 10-13, 15, 16, 19, 20, 28, 29, 31, 32, 35-51 Neg; HI/Group A 1, 2, 4, 5 Neg; Group B 3, 7, 11, 15, 17, 23, 26, 27, 31, 33, 35, 37 Group C 6, 8 Neg 7 (+1/10); Group Patois 1, 2, Neg; Group Bunyamwera 1-3, 6-10, 13 Neg; 12 (+1/10); Group Phlebotomus 1, 2, 4-6, 8, 11 Neg; Group Simbu 2-4 Neg, 8 (+1/10); Minor Groups 2, 2b, 3, 4, 4a, 10a 15, 15a 15b Neg; Ungrouped 32, 36, 43, Neg; Group Capim 4 Neg;	Neg	Neg	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)	Bacterial Sterility	Mycoplasma	Refer.
V-503-701-562	Phlebotomus Fever	Sicilian	Sabin	Other arboviruses (Test/Virus/Titer) CF/Group Simbu 1-9 Neg; Group Bunyamwera 2, 3, 6-9, 11, 16 Neg; Group Tacaribe 1, 2, 5-7 Neg; Group Phlebotomus 2 (8/8), 1, 5-7, 11 Neg; HI/Group A 1-10, 12, 13, 15, 16, 19 Neg Group B 2-7 Neg; Group C 3, 5-10 Neg; Group Simbu 3, 4, 8, 10 Neg; Group Phlebotomus 1, 2, 4-6, 8, 11, Neg; Group Guama 3, 4 Neg; Group California 2 Neg; Group Tutlock 15 Neg; Group Capim 4 Neg;	Neg	Neg	--
V-505-701-562	Simbu	Oropouche	TRV1 9760	Other arboviruses (Test/Virus/Titer) CF/Bunyamwera - unassigned 1 Neg; Group Capim 1 Neg; Group Patois 1 Neg; Group Guama 1 Neg; Small Groups 6-8, 9a, 9d, 10, 10a, 11a, 13, 14a, 16 16a, 16b, Group VSV 4 Neg; Ungrouped 1, 2, 8, 10-13, 15, 16, 19, 20, 28, 29 31, 32, 35-51 Neg; HI/Group A 1, 2, 4, 5 Neg; Group B 3, 7, 11, 15, 17 23, 26, 27, 31, 33, 35, 37 Neg; Group C 6, 8, Neg; Group Patois 1, 2, Neg; Group Bunyamwera 1-3, 6-10, 12, 13 Neg; Group Phlebotomus 1, 2, 4-6, 8, 11 Neg; Group Simbu 2, 3, 8 Neg; Minor Groups 2, 2b, 3, 4, 4a, 10a, 15, 15a, 15b Neg; Ungrouped 32, 36, 43, Neg; Group California 2, 6, 9, 10 Neg; Group Capim 4 Neg.	Neg	Neg	--
V-506-701-562	Ungrouped	Colorado Tick Fever	Florio	Other Arboviruses (Virus/Test/Titer) CF/Group Simbu 1-9 Neg; Group Bunyamwera 2, 3, 6, 8, 9, 11, 16 Neg; Group Tacaribe 1, 2, 5, 7 Neg.	Neg	Neg	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)		Bacterial Sterility	Mycoplasma	Refer.
V-509-701-562	B	Ilheus	TRVL 5800	Other viruses (Test/Virus/Titer)	CF/Group B 3 (4/4); 1, 4, 7 (8/4); 31 (8/16); 17, 23 (16/16); 6, 11, 35, 36, 37 (<1/4) Group A 3, 4, 6, 17, 20 Neg; Group Bunyamwera 2, 3, 9, 11, 16 Ngg; Group C 7 Neg; Group Guama 1-5 Neg; Group Patois 1 Neg; Group Changuinola 1, 2 Neg; Group Simbu 2, Neg; Group Phlebotomous 4, 7 Neg; Minor Groups 2, 3, 3a, 7, 8, 13, 15, 16 16a, 16b, 24 Qalyub Neg; Ungrouped 11 Neg; HI/Group B 7 (640); 23 (320); 31, 33 (160); 1, 3, 36 (80); 4 (40); 11, 17 (10); 6, 35, 37 (<10)	Neg	--	--
V-510-701-562	Guama	Guama	TRVL 33579	Other viruses (Test/Virus/Titer)	CF/Group A 3, 4, 6, 17, 20 Neg; Group B 7, 11, 15, 27, 28, 31, 33, 35-37 Neg; Group C 7 Neg; Group Patois 1, 2 Neg; Group Bunyamwera 2, 3, 9, 11, 13, 16 Neg; Group Simbu 2 Neg; Group Phlebotomus 4, 7 Neg; Group Changuinola 2 Neg; Minor Groups 2, 3, 3a, 7, 8, 13, 15, 16, 16a, 16b Neg; Ungrouped 11 Neg;	Neg	--	--
V-511-701-562	California	Melao	TRVL 9375	Other viruses (Test/Virus/Titer)	CF/Group California: 7(4/64); 2-4, 9, 10 (8/64) Group A: 3, 4, 6, 17, 20 Neg; Group B 7, 11, 27, 28, 31, 33, 35-37 Neg; Group C 7 Neg; Group Bunyamwera 2, 3, 9, 11, 13, 15, 16 Neg; Group Guama: 2-5 Neg; Group Patois 1, 2 Neg; Group Simbu 2 Neg; Group Phelbotomous 4, 7 Neg Group Chinguinola 2 Neg; Minor Groups 2, 3, 3a, 7, 8, 15 Neg; Ungrouped 11 Neg;	Neg	--	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)	Bacterial Sterility	Mycoplasma	Refer.
V-534-70;-562	Simbu	Buttonwillow	A7956	Other arboviruses (Test/Virus/Titer)	CF/Group Simbu 3, 4, 5, 7 Neg. Turlock, EEE, SLE Neg Neg	--	--
V-701-511-570	Reovirus	1	Hull-5727	Other viruses (Test/Virus/Titer)	SN/Reo 2/1:32 - Reo 3/< 1:16 HI/Reo 2/1:16 - Reo 3/1:16 Neg	--	--
V-702-501-570	Reovirus	2	Jones	Other viruses (Test/Virus/Titer)	Sn/Reo 1/<1:16 - Reo 3/<1:16 HI/Reo 1/1:16 - Reo 3/<1:8 Neg	--	--
V-703-501-570	Reovirus	3	Abney	Other viruses (Test/Virus/Titer)	SN/Reo 1/1:128 - Reo 2/1:32 HI /Reo 1/1:16 - Reo 2/1:16 Neg	--	--

Catalog #	Virus Group	Type	Strain	Other Viruses (Virus/test/titer)	Bacterial Sterility	Mycoplasma	Refer.
G-201-701-567	C	Grouping Ascitic Fluid	--	Other arboviruses (Test/Virus/Titer)	CF/Group Simbu: 1-9-Neg (1:16)*; Group Bunyamwera: 2, 3, 6-9, 11, 16 Neg (1:10	Neg	--	--
G-203-701-567	Simbu	Grouping Ascitic Fluid	--	Other arboviruses (Test/Virus/Titer)	CF/Group Bunyamwera 2, 3, 6-9, 11, 16 Neg; Group Tacaribe 1, 2, 5-7, Neg.	Neg	Neg	--
G-205-701-567	Bunyamwera	Grouping Ascitic Fluid	--	Other arboviruses (Test/Virus/Titer)	CF/Group Simbu 1-3, 5-9 Neg; 4(1/4); Group Tacaribe 1, 2, 5-7 Neg. HI/Group A 1-10, 12, 13, 15, 16, 19 20 Neg; Group B 2-7 Neg; Group C 3, 5-10 Neg; Group Phlebotomous 1, 2, 4-6, 8, 11, Neg; Group Guama 3, 4 Neg; Group Simbu 3, 4, 8, 10, Neg; Group Capim 4 Neg;	Neg	Neg	--
G-209-701-567	A	Grouping Ascitic Fluid	--	Other arboviruses (Test/Virus/Titer)	CF/Group Simbu 4, 8 Neg; 1, 6-(1/4); 2, 3, 5, 7 9-(1/4); Group Bunyamwera 3, 6, 8, 11, 16-(1/4); 2, 9-(1/4); Group Tacaribe 1, 2, 5-7 Neg; HI/Group B 2-7 Neg; Group C 3, 5-9 Neg; Group California 2 Neg; Group Simbu 3, 4, 8 Neg; Group Phlebotomus 1, 2, 4-7, 8, 11, Neg; Group Bunyamwera 1-3, 6-18, 17 Neg Group Guama 3, 4 Neg; Group Turlock 1 Neg; Group Capim 4 Neg; Group Simbu 10 Neg;	Neg	Neg	--
G-215-701-567	Group Capim	Grouping Ascitic Fluid	--	Other arboviruses (Test/Virus/Titer)	CF/Group Bunyamwera 2, 11, 16 Neg; California, Quaranfil, Guama, Ilheus Neg;	Neg	--	--

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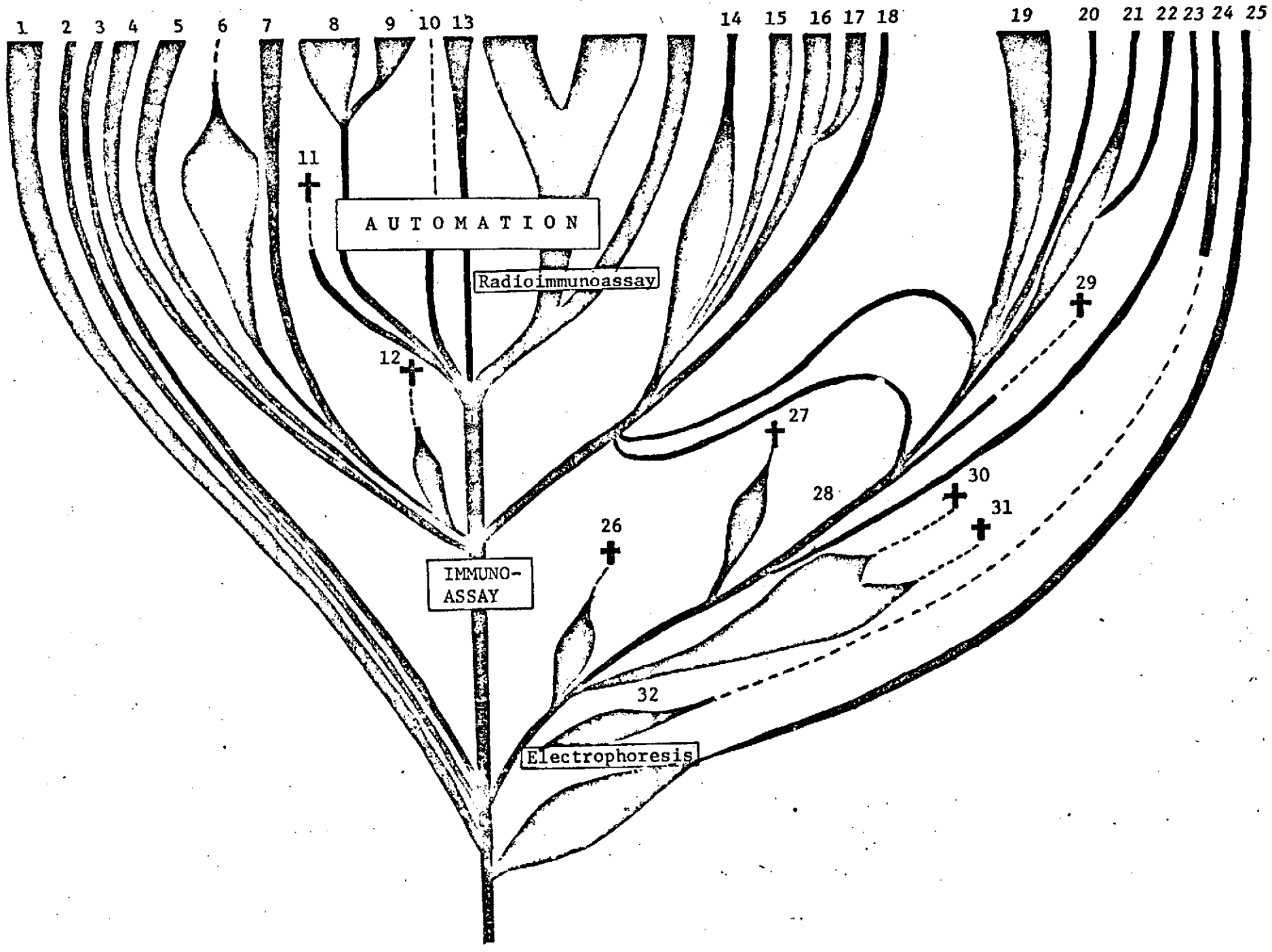
APPENDIX 8

GRAPH OF ELECTROPHORESIS EVOLUTION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AUTOMATION
Radioimmunoassay
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IMMUNO-
ASSAY
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Electrophoresis

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2. viscometry
3. refractometry
4. hemaglutination
5. immunofluorescence
6. radioimmunoassay diffusion
7. ouchterlong
8. direct nephelometry
9. inhibition nephelometry
10. hemagl. inhibition
11. turbidimetry
12. oudin
13. polarization fluorescence
14. immunoelectrophoresis
15. immunofixation
16. counter electrophoresis
17. "capture zone"
18. crossed antigen-antibody electrophoresis
19. rehydratable film
20. variable EOM
21. acrylamide
22. isotachophoresis
23. pevicon
24. isoelectric focusing
25. chemical and precipitation techniques
26. paper
27. agar
28. agarose gel
29. starch
30. cellulose acetate "mini"
31. cellulose acetate "standard"
32 free